PREVALENCE OF METABOLIC SYNDROME USING IDF CRITERIA IN PATIENTS WITH PREMATURE CORONARY ARTERY DISEASE PROVEN BY CORONARY ANGIOGRAM

By

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In partial fulfilment of the requirements for the degree of

Doctor of Medicine in General Medicine

Under the guidance of

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April 2014

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This is to certify that the dissertation entitled, **"PREVALENCE OF METABOLIC SYNDROME USING IDF CRITERIA IN PATIENTS WITH PREMATURE CORONARY ARTERY DISEASE PROVEN BY CORONARY ANGIOGRAM**" is a bonafide original work of **Dr.VARUN.S** in partial fulfilment of the requirements for the degree of Doctor of Medicine in General Medicine

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I hereby declare that this dissertation entitled **"PREVALENCE OF METABOLIC SYNDROME USING IDF CRITERIA IN PATIENTS WITH PREMATURE CORONARY ARTERY DISEASE PROVEN BY CORONARY ANGIOGRAM"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. VARUN.S** under the guidance of **Dr.Sujaya Menon M.D MRCP,** Professor of Medicine, P.S.G IMSR, Coimbatore.

This dissertation is submitted to the Tamil Nadu Dr. M.G.R Medical University in fulfilment of the University regulations for the award of MD degree in General Medicine. This dissertation has not been submitted for award of any other degree or diploma.

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March 27, 2014

To
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The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore -4, has reviewed your proposal on March 21, 2014 in its expedited review meeting held at IHEC Secretariat, PSG IMS&R, between 10.00 am and 11.00 am, and discussed your study proposal entitled:

"A study on prevalence of metabolic syndrome in premature coronary artery disease proven by coronary angiogram using IDF criteria"

The following documents were received for review:

1. Duly filled application form
2. Proposal
3. Informed consent forms
4. Data collection tool
5. CV
6. Budget

After due consideration, the Committee has decided to approve the study.

The members who attended the meeting at which your study proposal was discussed are as follows:

Name	Qualification	Responsibility in IHEC	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
Dr P Sathyan	DO, DNB	Clinician, Chairperson	Male	No	Yes
Dr S Bhu\vaneshwari	M.D	Clinical Pharmacologist Member - Secretary	Female	Yes	Yes
Dr Sudha Ramalingam	M.D	Epidemiologist Alt. Member - Secretary	Female	Yes	Yes
Dr Y S Sivan	Ph D	Member –Social Scientist	Male	Yes	Yes
Dr D Vijaya	Ph D	Member – Basic Scientist	Female	Yes	Yes

The approval is valid for one year.

We request you to intimate the date of initiation of the study to IHEC, PSG IMS&R and also, after completion of the project, please submit completion report to IHEC.

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This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Yours truly,

27.3.17

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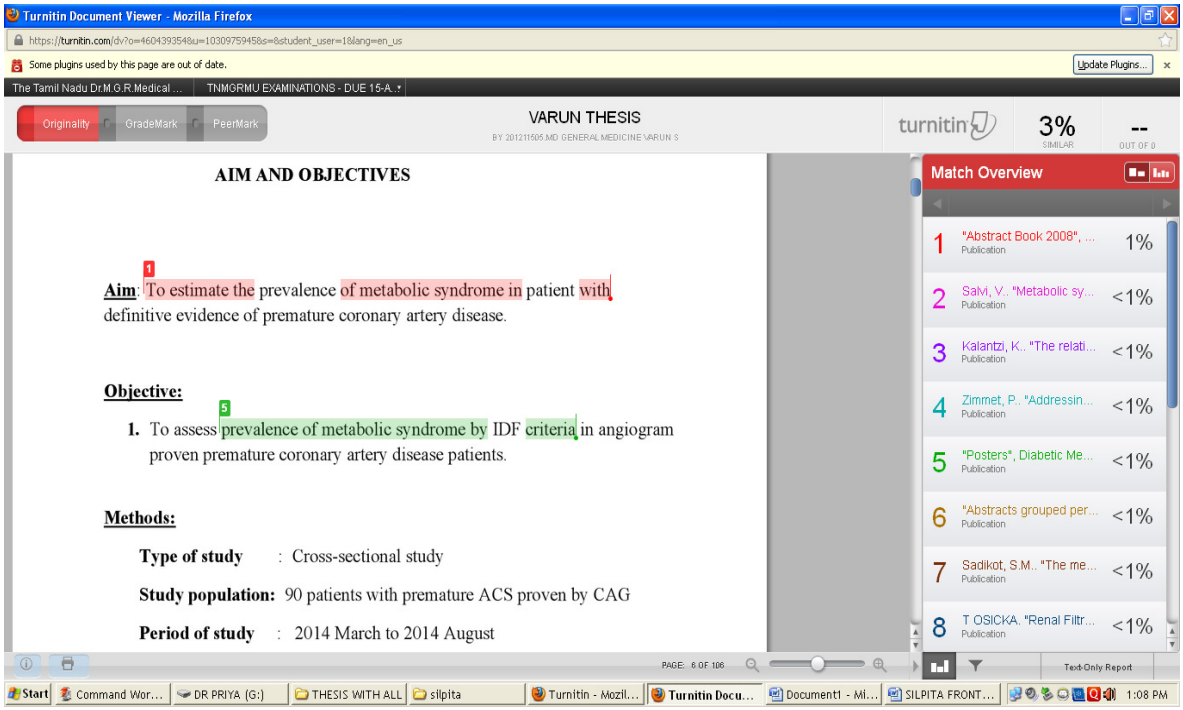
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Aim: To estimate the prevalence of metabolic syndrome in patient with definitive evidence of premature coronary artery disease.
Objective:
1. To assess prevalence of metabolic syndrome by IDF criteria in angiogram proven premature coronary artery disease patients.
Methods:
Type of study : Cross-sectional study
Study population: 90 patients with premature ACS proven by CAG
Period of study : 2014 March to 2014 August

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OBJECTIVES OF THE STUDY:

To evaluate the prevalence of metabolic syndrome using IDF criteria in premature coronary artery disease proven by coronary angiogram.

METHODS:

Patients under 45yrs of age who were diagnosed to have acute coronary syndrome proven by coronary angiogram will be included in this study. The eligible subjects are explained about the study and after getting consent will be evaluated for metabolic syndrome parameters(using IDF criteria) and subjected for thorough clinical examination. All the collected data will be analyzed and the important findings of the study will be highlighted.

RESULTS:

1. Patients with metabolic syndrome had an average HDL-cholesterol level of about 32.36, whereas in non-MS group the average value was 36.78,with p value of <0.05 which is statistically significant

2. The average triglyceride value in MS group was 179.14,whereas in non-MS group it was 115.86,with p value of <0.01 which is statistically significant.

3. Fasting blood glucose was high in 43 patients (64.17%) in MS group, whereas it was high only in 9 patients (39.13%) of the non-MS group with the p-value of <0.05 which is statistically significant.

4. 44 patients (65.67%) of the MS-group and only 6 patients (26.08%) of the non-MS group had elevated blood pressure of more than 130/85mmHg, with the p-value of <0.01 which is statistically significant.

5. Average WC of patients in MS group and non-MS group were 95.64 and 87.23respectively. The p-value came as <0.001 which is statistically very significant.

6. Patients (46.26%) with MS were found to have pre-existing hypertension compared to 3 (13.04%) in non-MS patients. The p-value obtained was <0.01, which is statistically significant.

7. 10 Patients (14.92%) in the MS group and 2 patients(8.69%) in the non-MS group had history suggestive of CAD in the family.

8. 42 patients (62.68%) in MS group and 15patients (65.21%) in non-MS group were smokers with p-value of 0.825(not significant)

9. 32 patients (47.76%) in MS group and 13 patients(56.52%) in non MS group were alcoholic. p-value obtained was 0.468 which is statistically not significant.

10. 36 (53.7%) out of 67 patients in MS group presented with ST elevation MI, whereas it is 18(78.26%) out of 23 in NON MS with the p value of 0.03 which is statistically significant (this may be attributed to occlusion of the vessel by emboli in N-MS group but whereas in MS atherosclerotic occlusion of the vessel is more common than embolic).

11. 23 (34.32%) out of 67 patients in MS group and 11(47.82%) out of 23 in NON MS group had LV dysfunction with the p value of 0.24, which is statistically not significant.

CONCLUSION

- In our study, 90 cases of acute MI aged ≤ 45 were studied for metabolic syndrome using IDF criteria. MS was diagnosed in 67 of 90 cases studied.

- Waist circumference was followed by Diabetes mellitus /Systemic hypertension/ elevated BP / hypertriglyceridemia/ elevated FBS and decrease in fasting HDL arranged in the order of prevalence in the study group which was statistically significant.

- Among the 67 patients, 14 met all criteria for MS, 24subjects had 4 and 29 subjects had 3 of 5 MS criteria, With WC ≥ 80 for females and ≥ 90 for males being a definite criterion.

- The prevalence of alcohol, whether a smoker ,history of CAD in the family, dyslipidemia , and vessel involvement – SVD/DVD/TVD were same for both MS and non MS group.

- Thus it is obvious that MS predominates over other conventional criteria or scores in estimating the risk of developing MI and related complications and its prevalence in our study population is 74.4% which is very significant.

- Though people living in low income countries like India have lower risk factor for CVD, compared with high income countries, the rate of death due to CVD is highest in low income countries. This is because there is better control of risk factor due to frequent use of proven drugs to reduce the risk of deaths.

- Thus determinants like easy and timely access to health care and medicine, diagnosis of risk factor and treatment / control and greater awareness play an important role in preventing death. Hence the two means to counter the risk factors and decrease the mortality are health promotion and health care.

- Health promotion component is to raise awareness and risk reduction. This is better done by identifying at risk individuals by the presence of MS component in this group and providing health care facilities for early detection and effective treatment in order to prevent cardiovascular disease morbidity and mortality.

- From the study it is clear that IDF consensus definition for MS suits Indians best for identifying high risk individuals. Hence we recommend its use to help prevent CVD morbidity and mortality in younger individuals in whom it is difficult to estimate CVD risk.

- As the risk factors have an increasing trend in India so does the mortality. The cardiovascular crisis is waiting to worsen unless we improve the health care system.

- Hence risk factor modification, regular physical activity and healthy diet among young patients should be emphasised for primary prevention of CAD.

- The concept of metabolic syndrome is very important as it provides simple and comprehensive information to the public.The medical professional should assess for presence of all the MS parameters whenever necessary.

INTRODUCTION

Coronary artery disease affecting younger individuals has reached enormous proportions. There is of no doubt that it will become a major public health problem in future unless we concentrate on reversible cause and prevention through research studies[1].Most common cause for myocardial infarction is coronary artery thrombosis, secondary to atherosclerosis[2].Metabolic syndrome (MS) refers to a constellation of complex inter related risk factors for cardiovascular disease and diabetes which appears to directly promote the development of atherosclerotic cardiovascular disease[3].The syndrome X (MS) represents a combination of multiple risk factors like central adiposity, hypertension, dysglycemia due to development of insulin resistance, lipid abnormalities like elevated triglycerides, low HDL (high density lipoprotein) cholesterol levels, pro-thrombotic and pro-inflammatory state in the same person which occur together more frequently than predicted by chance alone[4]

The prevalence of metabolic syndrome in Indian varies from region to region. A recent review on insulin resistance syndrome showed a rapid increase in its development among Indians[5].Studies on patients with metabolic syndrome showed around six fold raise in cardiovascular mortality than compared to those without metabolic syndrome[6].

Though the association between MS and CVD is certain, the level of associated risk is not clearly defined due to difference in proposed definitions[7]

Traditional risk factors constitutes around half the risk of development of first myocardial insult, especially in Asian Indian population. The burden of cardiovascular disease is likely to increase in the incoming years with significant impact on the society[8].

For allocation of research and health resources it is essential for us to understand the dimensions of this metabolic syndrome as it can cause serious morbidity.

However fewer studies reported on the existence of MS among native Indian population based on epidemiological studies and almost only very few studies are available on its prevalence in younger individuals with significant cardiovascular morbidity. This is important especially in country like India with a large number of diabetic patients[9].

Early intervention in patients with metabolic syndrome with intensive approach to lifestyle and behaviour modification in the form of diet, exercises and drugs may prevent the development of cardiovascular disease in the future.

In our study we have used International Diabetes Federation criteria (which have race and ethnic specific waist circumference cut-off points) in order to know MS prevalence in premature coronary artery disease patients proved by angiogram. This may help in providing direction for future research and health intervention.

Patients with MS are at increased risk of developing cardiovascular disease and are also associated with increased mortality and morbidity, which makes a clear understanding of this problem, is vital for allocation of resources and health care. Traditional risk factors together constitute approximately half of the chance of developing a first episode of MI, especially among Asian Indian population. As a result, both incidence and prevalence of cardiovascular disease is likely to increase in the incoming years with significant socio-economic consequences.

However regarding the prevalence of MS as a whole in the native Indian population only few studies are available based on epidemiological studies and almost no studies are available on its prevalence in younger individuals with significant cardiovascular morbidity.

Early intervention to the MS patients by means of intensive lifestyle and behaviour modification in the form of diet, exercises and drugs may prevent the future development of cardiovascular disease like myocardial infarction.

To know the actual burden of MS in the community this study has been undertaken to find the exact distribution of MS in those with atherosclerotic coronary vascular disease proven by angiogram through the definition framed by International Diabetes Federation as this appears to be ideal in Indian setup. This may help in providing direction for future research.

AIM

Aim: To estimate the prevalence of metabolic syndrome in patient with definitive evidence of premature coronary artery disease.

Objective:

To assess prevalence of metabolic syndrome by IDF criteria in angiogram proven premature coronary artery disease patients.

Methods:

Type of study : Cross-sectional study

Study population: 90 patients with premature ACS proven by CAG

Period of study : 2014 March to 2014 August

Inclusion criteria:

1. Coronary artery disease proven by coronary angiogram (STEMI / NSTEMI / UA)
2. Age ≤ 45 years.

Exclusion criteria:

1. Patients who did not undergo coronary angiogram.
2. Age >45 years. Age < 18 years

REVIEW OF LITERATURE

The concept of metabolic syndrome was initially put forth by Kylin in 1920, who was a physician from Sweden. He described MS as combination of hyperglycemia, hypertension, and gout[10].

In the year 1947, Vague gave importance to upper body obesity as it was the phenotype he found most commonly associated with type 2 diabetes mellitus and cardio vascular disease[11].

In the year 1988 Reaven proposed the concept of Syndrome X that included resistance to insulin mediated glucose uptake, hyperglycemia, hyper-insulinemia, high blood pressure, hypertriglyceridemia, an increased VLDL cholesterol, and a decreased HDL cholesterol levels (high density lipoprotein). It was during this period hypertension, diabetes and cardio vascular disease drew much attention[12]

Till this period there were no specific criteria for diagnosing syndrome X. Obesity or visceral obesity was not included in any of the criteria described previously. Later, Lemieux proposed that hypertriglyceridemia and visceral obesity be considered as a principle component of MS[13, 14.]

The WHO in 1998 suggested a specific definition of metabolic syndrome which was improved in due course of time after various research studies and analyse by many organizations and professional bodies.

After crossing various stages of improvisation we now describe MS as a confluence of many classical risk factors for cardiovascular disease such as central obesity, increased blood glucose, elevated blood pressure, hypertriglyceridemia and low HDL-cholesterol levels. In the analysis even after excluding diabetes patients, MS patients were found to have had more than 2 fold raise in adverse cardiovascular disease events[15, 16, 17].

Though middle aged and eldery individuals are more prone to develop CAD, studies showed that there is an increasing evidence of its occurrence in young individuals, resulting in premature death and disability[18, 19, 20].

Acute coronary syndrome (ACS) in young patients differs from that in older individuals in terms of risk profile and mortality[21].

Presence of MS in an individual reflects an increased chance of developing atherosclerotic vascular disease and thereby it will be helpful in identifying high cardiovascular disease risk individuals. In a cross-

sectional study it was found that more and more number of adults (>1/3) and children were found to have MS according to the proposed MS diagnostic criteria, and its distribution in patient with coronary artery disease seems increasing proportionately. But there are not many studies available on CAD patients less than 45 years with regard to MS prevalence[22,23,24,25,26].

The DECODE study says that, there is an increasing evidence regarding patient with low score for cardiovascular disease risk and MS have increased chance of developing fatal cardiovascular disease events than those without MS[27].

Epidemiological research has identified risk factors that increase the likelihood of coronary heart disease events. Management of risk factors can improve coronary endothelial function, stop the progression of atherosclerosis, prevent disruption and thrombosis of vulnerable atherosclerotic plaque and reduce coronary heart disease morbidity and mortality. When risk factors co-exist, they multiply the risk of coronary heart disease several fold.

A recent Bethesda conference proposed a classification scheme according to the strength of evidence that risk factor intervention favorably affects outcome. It is difficult to find too many risk factors in young patients who developed coronary artery disease. MS more

commonly present in these patients. This should be practiced even in those subjects at low risk of developing cardiovascular disease. The recognition of MS will definitely be important in diagnosing patient with high risk of developing cardiovascular disease more so than estimated by other conventional cardiovascular risk scores.

METABOLIC SYNDROME (MS)

Obesity, especially abdominal obesity, is associated with insulin resistance on utilization of fatty acid and glucose at the peripheries which results in development of diabetes. This resistance to insulin along with adipocyte cytokines, hyper-insulinemia and hyperglycaemia may lead to an abnormal lipid profile, hypertension, vascular inflammation and vascular endothelial dysfunction, that will lead on to atherosclerotic cardiovascular disease[28,29,30,31].

In the past MS has been called by different names- the obesity dyslipidemia syndrome, New world syndrome, Multiple syndrome, IR syndrome, syndrome X, the deadly quartet [32]

Table.1 Various terminologies used to describe MS[18]
• Atherothrombogenic Syndrome • Beer-Belly Syndrome • Cardiovascular disease syndrome • Chronic cardiovascular risk factor clustering syndrome • Deadly quartet • DysMETS • IR syndrome • Metabolic cardiovascular syndrome • METS • Multiple syndrome • Multiple METS • PluriMETS • Reaven's syndrome • Syndrome X • New world syndrome

Genetic predisposition, body fat distribution and lack of exercise, will affect the likelihood of development of diabetes and CVD in obese subjects. So each of its individual component has to be identified correctly and treated effectively to reduce adverse outcome related to diabetes mellitus and CVD[33,34]

DEFINITION

There are many definitions for the metabolic syndrome. It represents the clustering of risk factors for diabetes and cardiovascular disease. These risk factors comprise glucose intolerance, hypertension, hypertriglyceridemia, low levels of HDL cholesterol and central obesity. Despite its growing prevalence worldwide there is still a lack of uniformity in accepted definitions and controversy regarding the pathogenesis of metabolic syndrome. Thus it remains an evolving concept with different working groups defining varied criteria for the condition.

The various criteria proposed by different professional bodies include those developed by the WHO[35], which used WHR to measure central obesity; the European Group for the Study of Insulin Resistance[37] which is a modification of WHO, used insulin resistance; this was followed by the NCEP ATP III [36]. The used WC instead of [WHR] for quantifying central obesity. The confusions which developed while establishing parameters to diagnose MS with lack of consensus on fixing cut-offs for WC led to the development of IDF (International Diabetes Federation) [38] and the modified ATP III definition[39].

Several other metabolic abnormalities have also been found to be linked with this syndrome namely hyperuricemia, disorders of

haemostasis, microalbuminuria and elevated levels of proinsulin and leptin, elevated levels of PAL-1 factor VII fibrinogen and Vwf.

Coexistence of these factors is labelled metabolic syndrome. The clustering together of all these risk factors tend to accelerate the development of atherosclerosis and increases the risk for cardiovascular morbidity and mortality. The presence of metabolic syndrome confers a 2-fold increase in risk of major CVD events and 5-fold increase in risk for type 2 DM. The metabolic syndrome has also been identified as precursor state of non-alcoholic fatty liver disease, chronic kidney disease and chronic lung disease. Knowledge of these abnormalities has several therapeutic implications.

The various definitions of the metabolic syndrome are as follows. The National Cholesterol Education Program (NCEP/ATP III) is the most widely used[39].

WHO DEFINITION

In 1999, WHO proposed a definition for MS. According to this presence of IGT or DM, and or resistance to insulin with any two or more than two of the following criteria defines MS, which includes,

1. Increased arterial pressure ≥140/90 mmHg

2. Raised plasma triglycerides (≥150mg/dl) and / or low HDL-C (<39mg/dl)

3. Abdominal obesity with WHR more than 0.9 and 0.85 in men and women or BMI>30kilogram/meter square.

4. Presence of micro-albumin in urine of ≥ 20µg/min or albumin creatinine ratio of ≥ 30/mg/gm creatinine.

EUROPEAN GROUP FOR STUDY OF INSULIN RESISTANCE

DEFINITION

The EGIR definition of MS was a modified version of WHO which used IR in the place of MS. As per EGIR to diagnose IR plasma insulin should be high i.e. greater than the 75 percentile, together with any two of the following parameters

1. Abdominal adiposity with WC ≥94cms and ≥80 cms in men and women.
2. High blood pressure, more than or equal to 140/90 mmHg or on any anti-hypertensive drugs for systemic hypertension.
3. Hypertriglyceridemia (≥150mg/dl) and /or low HDL-cholesterol levels (<39mg/dl) in both the sexes
4. IGT/IFG, but should not be a diabetic.

NCEP ATP III DEFINITION

NCEP ATP III developed guidelines based on factors which influence high risk of developing cardiovascular disease[40]. This was modified by AHA and NHLBI in the year 2005[41,42] .

It includes the following

- Lowered FBG cut-off to 100 mg/dl,
- Diabetics were included in the criteria
- To make the process simple in diagnosing MS, NCEP ATP III proposed a definition which used WC in place of WHR for quantifying central obesity
- Patients on lipid lowering and anti-hypertensive drugs were included in the criteria
- As per this patient is considered to have MS if at least any of the following 3 criteria is present:
- Waist circumference $\geq$ 102 cms and $\geq$ 88 cm for men and women
- Hyper triglyceridemia: $\geq$ 150 mg/dl or on lipid lowering drugs for hypertriglyceridemia
- Low HDL –C: <40 mg/dl and <50 mg/dl for for men and women or treatment for the same.

- High systolic blood pressure ≥130 mmHg or diastolic ≥ 85mmHg or receiving treatment for high blood pressure
- High fasting glucose ≥110 mg/dl or receiving treatment for elevated blood glucose.

According to NCEP ATP III abdominal adiposity is considered more important than generalised adiposity and WC was included and body mass index from the definition. The term IRS was proposed as they believed IR is not a principal component for developing MS.

For quantification of abdominal obesity NCEP ATP III used WC and omitted WHR as suggested by WHO. They put low HDL and hypertriglyceridemia as two discrete parameter in the criteria because each has a major role in development of CVD and diabetes. They excluded parameters like microalbuminuria from the criteria which made diagnosis of MS easy. They also reduced the cut-off points for hypertension and HDL cholesterol levels. Though NCEP considered MS as a pro inflammatory state, they did not include this in the criteria for defining MS. Previously there was always a difficulty in applying all the above criteria in different ethnic groups and races due to significant difference in the WC among them (including Asians).

IDF-DEFINITION

IDF proposed MS definition based on ethnic and race specific WC cut-off and updated their MS criteria in the year 2006 [43]. According to the IDF, patient is considered to have MS if any three of the following criteria is present with abdominal adiposity as a principle component (with ethnic and race specific cut off for WC)

The race and gender specific waist circumference cut-offs suggested are as follows:

TABLE 2: WAIST CIRCUMFERENCE IN GENDER AND RACE SPECIFIC GROUPS

Country	WC cut-off	
Europeans Americans [continue using NCEP ATP III values (102cm for M & 88cm for F)]	for Males in cm ≥ 94	for Females in cm ≥ 80
Asians especially South Asians based on a Asian-Indian & Chinese, population	≥90	≥80
China	≥90	≥80
Japan	≥90	≥80
South-Americans and Central America	Use south Asian WC data	
Africans	Use European WC data	
Mediterranean and Middle east	Use European WC data	

CRITERIA:

- Hypertriglyceridemia ≥ 150 mg/dl or on lipid lowering drugs for the same.
- Decreased HDL levels <40 mg/dl and <50 mg/dl in men and women, or on drugs for this same abnormality
- Increased Systolic Blood Pressure ≥ 130, and diastolic Blood Pressure ≥ 85, or on anti-hypertensive for the same (SHT).
- FBS ≥ 100 mg/dl, or known case of diabetes mellitus and on drugs for the same.

The ADA and European association for diabetic study suggested that, to tag a person having MS does not confers any additional risk than contribution by any of its individual parameter.

COMPARISON

TABLE 3: THE CURRENT DEFINITIONS APPLIED BY THREEDIFFERENT ORGANISATIONS

		WHO 1999	NCEP / ATP III 2005	IDF 2005
S.No	Criteria required	1st/5th with >2 other criteria	Any 3 criteria	2nd+ any 2 other criteria
1.	Insulin resistance	Yes	-	-
2.	Obesity	WHR : male >0.9 female > 0.85, body mass index >30	WC : Male >102 female >88	Ethnicity specific
3.	Lipid	TG>150mg or HDL<35(M),<39(F)	TG>150mg or HDL<50(M),<40(F)	TG>150mg or HDL<50(M),<40(F)
4.	Blood pressure	>140/90mmHg	>130/85mmHg or on therapy	>130/85mmHg or on therapy
5.	Glucose	T2DM IGT IFG	Fasting >100mg/dl or DM	Fasting >100mg/dl or DM
6.	Other	Microalbuminuria	-	-

From the NHNES survey database started in 1999 regarding prevalence of MS in American adults 39% had MS by IDF criteria,33.5% had MS by NCEP ATP III criteria[44].And there is an overlap in 93 percent of subjects making it difficult to diagnose MS in those patients. When the same was applied to a city dwelling population it was found that more than 18% of subjects were found to have MS than compared to those diagnosed by NCEP ATP III[45].From an epidemiological study on urban and rural Chennai population (CURES) MS was diagnosed in 23% of patients studied via WHO criteria, 18% with NCEP ATP III criteria and 25.8% with the help of IDF criteria but only 224 patients were diagnosed to have had MS when all three criteria were applied[46].

When levels of inflammatory markers like CRP, PAI-1, and IL-6 are elevated ,they result in high risk of developing CVD and diabetes [47-53]. But the association between the metabolic syndrome and elevated CRP levels was not demonstrated in a study on phenotype patterns and its relation with the MS [54]. Hence whether to treat this pro-inflammatory state in the background of metabolic syndrome is not known.AHA/CDC guidelines suggested that C-reactive protein levels can be tested based on clinical judgment and should be optional and not recommended routinely[55].

CONTRIBUTION OF THE INDIVIDUAL RISK FACTORS TO THE GENESIS OF CV RISK IN METABOLIC SYNDROME

OBESITY

Overweight and obesity are increasing in our population. No group is exempt from developing obesity; it occurs in all age groups and all genders. In Asian–Indians, subcutaneous fat depots and abdominal obesity predispose to metabolic syndrome and insulin resistance. Abdominal obesity is characterised by increased WC and WHR. However in Asian-Indians the waist circumference may not be that large but abdominal obesity is prominent. Enlarged adipocytes are related to development of IR and predisposes to diabetes mellitus contributing to CVD risk in patients with metabolic syndrome[56].

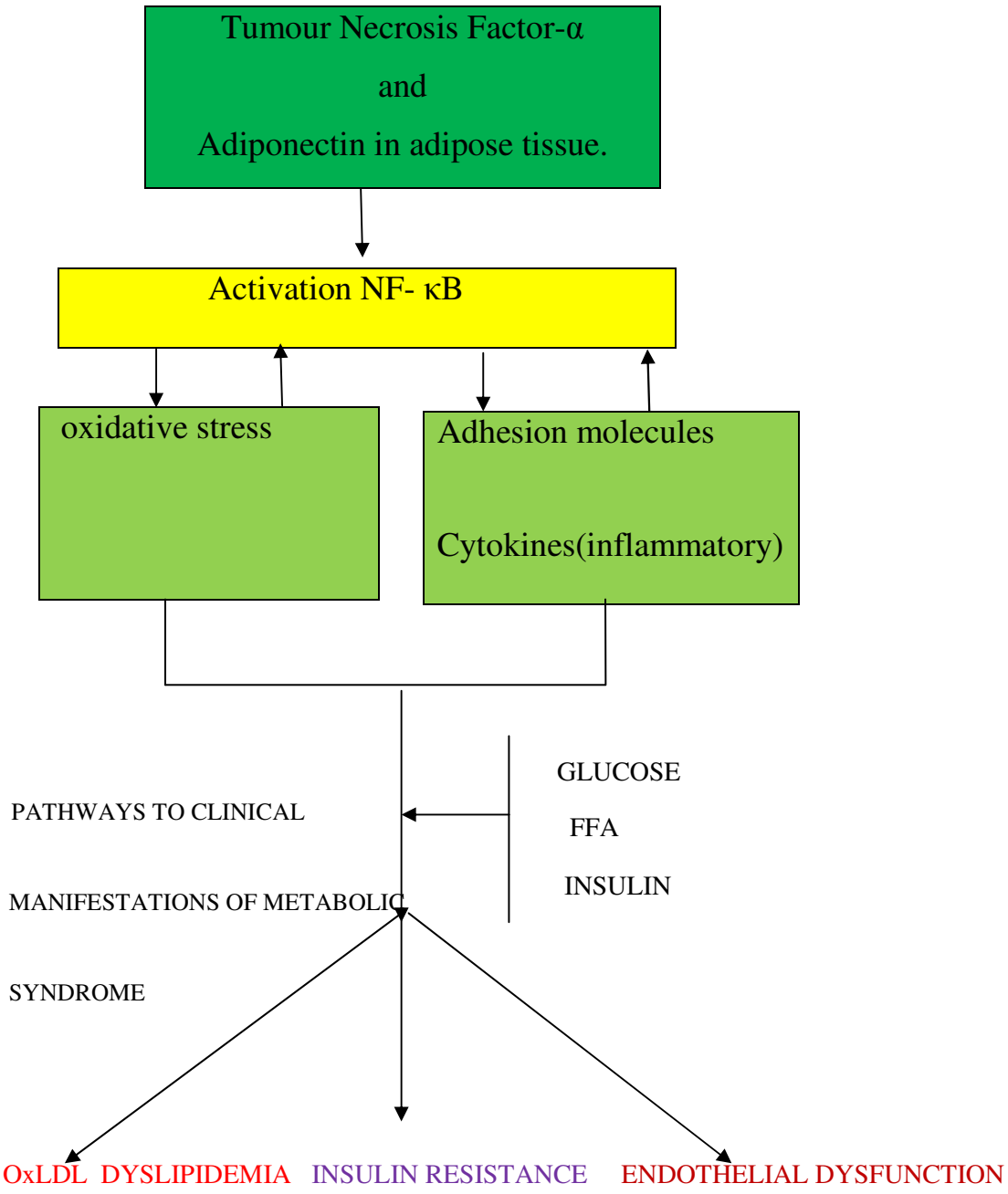
ROLE OF ADIPOCYTES IN THE DEVELOPMENT OF METABOLIC SYNDROME

Visceral fat is metabolically more active when compared to subcutaneous fat in the aspects of insulin sensitivity. Visceral adipose tissue will have histology and metabolism different from that of subcutaneous adipose tissue. It has adipocytes resistant to insulin and inflammatory cell infiltrates. Two hormones secreted by visceral adipose tissue appear to play a key role in generation of metabolic syndrome: TNFα and adiponectin. Expression of TNFα is increased during weight

gain and reduced during weight loss. TNFα and adiponectin have opposite action in the process of activating of NF- κB. This activated TNFα causes oxidative stress, which worsens the pathological process ending in oxidation of LDL and other lipid abnormalities, intolerance to glucose and resistance to insulin, elevated blood pressure, and damage to the endothelium and finally leads to the development of atherosclerosis. Endothelial damage and dysfunction is secondary to the NF- κB activation which when activated further results in recruitment of inflammatory cytokines and other molecules like VCAM, ICAM (adhesion molecules) which further aggravates the disease process. Further activation of NF- κB by increased levels of FFA, high glucose, and insulin levels in blood secondary to insulin resistance will alter natural metabolic process resulting in development of clinical manifestations of MS.

A phenotype with increased body fat with comparatively low BMI, decreased lean body mass especially in lower limbs , high body fat /body mass index ratio, increased WHR, sub scapular Vs triceps skin fold thickness and increased intramyocellular lipids has become more prevalent in Asians especially Indians[57].

Figure 1: Pathogenesis of MS



Pi-sunyer. Metabolic syndrome in obesity. Obesity Research 2004 vol. 12[58].

Increased body weight has a major role in the development of MS. The NHANES III Survey, it was found that the prevalence of MS in those who were of normal weight was 5 percent, it was 22 percent in overweight, and 60 percent in the obese[58, 59].

A 2.25 kg or more weight gain over 16 years increases the chance of getting MS 21 to 44 percent[60].

A large waist circumference alone can predict future risk of developing metabolic syndrome. It can identify about 46 percent of subjects who are likely to get MS in the near future especially within five years[61] making it necessary to implement primary prevention strategies by improving physical fitness and by reducing weight, targeting obesity[62,63]

Other factors — Factors like age, race, and weight, postmenopausal status, high carbohydrate diet, smoking, decreased physical inactivity, poor cardio respiratory fitness, soft drink consumption, drugs like clozapine all have their influence on development of metabolic syndrome[64,65,66].Genetic factors/family history of obesity accounts for around 50 percent chance of developing metabolic syndrome traits in offspring[67] .

HISTORY OF CAD

Though symptoms related to angina pectoris and myocardial infarction were seen from ancient times it came to light only in late 16th century which gave better understanding and knowledge on this disease. The first study on heart in the world perceiving the relation between the arrhythmia and loss of consciousness with an account of ischemia and myocardial infarction was put forth as a text in practica medicinalis by Bishop Thomas of Wroclaw (1297-1378)[100].

In the 18th century better knowledge of coronary vascular anatomy lead to the real discovery of IHD and MI by a physician who announced his observation in 1768. He was an English physician William Heberden (1710-1801till the 19th century it was named Heberden's disease after him.

Followed by Heberden, it was Ludwig Hekben, a pathologist in 1879 who confirmed that it was the thrombotic occlusion of the coronaries that was the primary pathology responsible for the development of MI[102.]

It was in the year 1910 that clinicians from Russia suspected possible acute MI in 5 patients[103]. In 1912 James Herrick insisted on strict

bed rest for treating patients with MI[104.] In 1919 he described the role of ECG in diagnosis of MI[105].

Better understanding of this disease in terms of patho-physiology and management was established in the year 1960 after many research studies. With a goal to study the life style of individuals residing in Framingham, USA to identify "Factors of Risk in the development of coronary artery disease", and to know the influence of various factor in the development of heart disease the Framingham Heart Study was established by NHLBI in the year 1948 [106].

From the study they found that

1. Patient with high arterial blood pressure and or increased level of cholesterol in blood are at increased risk of developing heart disease.
2. Higher incidence of myocardial infarction in women but the presentation was later when compared to men.

   Studying the risk factors causing atherosclerotic cardiovascular disease NHLBI suggested life style and behaviour modifications, and educated clinicians for better control of the disease in terms of mortality and morbidity[107]. Knowing the mechanism causing underlying pathology, NHLBI implemented prevention and control strategy by educating clinicians.

Many clinical studies were undertaken after understanding the concepts of this disease targeting control of blood pressure and cholesterol level through drugs by collaborating with various professional bodies in the community

CORONARY ATHEROSCLEROSIS

From various genetic and molecular studies it was clear that atherosclerosis develops secondary to long term inflammation of arteries which over a period of time forms an atheromatous plaque. The oxidative stress which acts as a trigger factor may be secondary to smoking, SHT, obesity etc. All these risk factors contributes to the alteration in endothelial permeability thereby causing endothelial injury. Exposure of sub endothelial collagen recruits lipid containing macrophages and other inflammatory cell which together with proliferation of endothelial smooth muscle cell and deposition of a fibrous collagen results in the formation of fibrous cap on to the growing atheromatous plaque. This atheromatous plaque when ruptured result in platelet aggregation at the local site plus release of other inflammatory mediators from platelets causing local vasospasm and activation of extrinsic coagulation cascade-forming complete occlusion of affected coronary vessel[134].

When the occlusion is chronic and incomplete it results in stable angina, unstable angina when it is complete but temporary and MI when the occlusion is permanent[129].

LDL cholesterol in plasma normally enters in to the cell through receptor mediated endocytosis which is clatherin mediated. When there is a defect in any of these the level of LDL will start rising in the blood. LDL has the capacity to take cholesterol to the peripheries and its level in blood is controlled by three different mechanisms.

1. Clatherin mediated engulfment of LDL receptor when it gets attached to the cholesterol molecule on the cell surface
2. Through LDL receptor recycling on the cell surface
3. Through negative regulation of receptor (feedback inhibition)

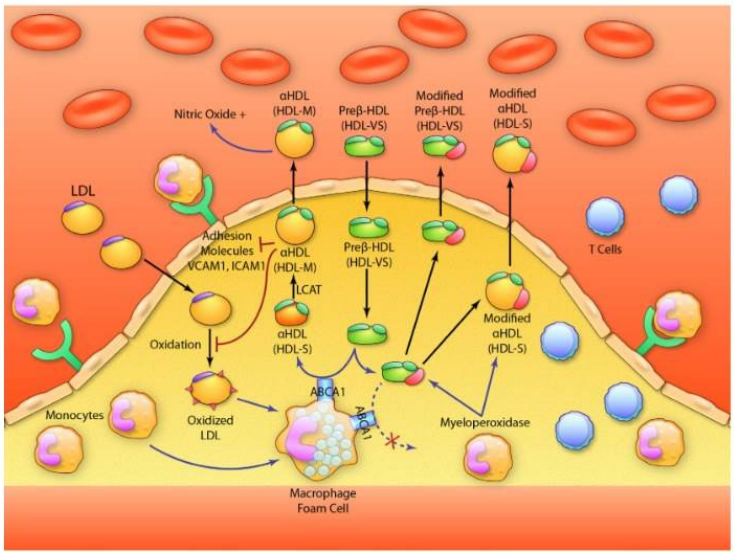
The LDL receptor was discovered by Goldstein and Brawn for which they received Nobel Prize in the year 1985[138]. This led to the discovery of statins by Akirra Endo which acts by inhibiting the enzyme HMG-CoA reductase [137].

Statins inhibits the enzyme HMG-CoA reductase resulting in decreased cholesterol synthesis (de novo) inside the body thus decreases the chance of developing MI[135,136].

Treatment with statins definitely prevent risk of getting MI in the future and improves survival rate but will not completely eliminate the development of CVD risk[141, 142]. There is always an inverse relation existing between HDL and development of atherosclerosis. This is because it contains large quantity of phospholipids which acts as a cholesterol acceptor and carries unlcassified cholesterol from peripheries to the liver there by preventing formation of atherosclerosis. It also has anti-inflammatory properties[143].

The drug nitric oxide which helps MI patient relieve symptoms by causing coronary vasodilatation was discovered by Fruchgot, Ignaro and Murrad for which they were awarded Nobel Prize in the year 1998[130-133].

FIGURE 2: ANTI THROMBOTIC PROPERTIES OF HDL



ABCA 1-ATP binding cassette protein A1; ICAM 1- intercellular adhesion molecule 1; HDL-M medium HDL particles; HDL-S small HDL particles

PREMATURE CAD

Coronary artery disease (CAD) can affect any age group, but its distribution in the younger age group is difficult to establish as most patients present with atypical symptoms. Many studies have defined young patients with coronary artery disease using age limit between 40 to 45 years as the cut-off.

Only limited data are available regarding myocardial infarction frequency in younger individuals. It was 12.9 per 1000 in men between the age of 30 - 34 years and 5.2 per 1000 in women between the age of 35 - 45 years from the analysis done by Framingham Heart Study[68] .

In other studies, the incidence of myocardial infarctions was found to be 4 to 10 percent in the age group of ≤ 40 or 45 years[69, 70, 71].

Though coronary heart disease is not very common in young individuals it has devastating effect on their lives. Myocardial infarction in young and older individuals may not be similar and differ in the aspects of clinical presentation, risk factor profile and prognosis.

Factors like cigarette smoking, family history, lipid abnormalities, diabetes, hypertension, obesity all contribute to the development of CAD. Among these cigarette smoking constitutes the most modifiable and very common risk factor prevalent in the age group of < 45 years[72-78].

Both genetic and environmental factors influence the evolution of CAD in young patients with a positive family history. In the offspring of young CAD patients the factors which probably accounts for the evolution of premature CAD are increased glucose, insulin and cholesterol levels in blood, excessive body weight. In a study done by Gaeta et al and Bao et al it was found that an increased incidence (62%) of a positive family history of coronary artery disease in young patients was noted in the report of 811 patients. Increased carotid intimal media thickening and endothelial dysfunction were more commonly seen in the offspring of patient with premature coronary artery disease[79, 80].

In a study carried out by Malmberg et al it was found that high triglyceride level and low level of high density lipoprotein were more prevalent in younger individuals. Though prevalence of hypercholesterolemia is similar in both younger and older age group it is hypertriglyceridemia which became the most common lipid abnormality inyoung patients with myocardial infarction as it presents with an intolerance to glucose and increased levels of small, atherogenic LDL (low density lipoprotein) particles in blood which results in development of atherosclerosis[81].

DIABETES AND HYPERTENSION

Most young patients have problems with metabolism of glucose. This is very important because impaired glucose tolerance has higher risk for coronary artery disease in patients without overt diabetes. On the other hand diabetes and hypertension seem to be less common in younger age groups].

In a study done by Mc Gill HC et al it was obvious that obesity is the prime factor responsible for development of atherosclerosis of coronary artery, but this is more commonly seen in young men than compared to women. LAD and RCA are prone to develop atherosclerotic lesion in young men with increased body mass index[82].

Framingham Heart Study reported that around 22 % of middle aged men and 14% of middle-aged women with obesity had coronary artery disease[83]

Mansouri et al and Chang et al found that contraceptive usage especially when combined with cigarette smoking, smoking marijuana, cocaine usage, factor-V Leiden mutation, all contribute to the development of coronary artery disease in young patients[86-89]

CLINICAL PRESENTATION

Most young patients do not have angina during initial presentation [90]. These were documented angiographically in a series of two hundred patients[91]. Young patients when compared to older individuals are more prone to develop acute coronary syndrome and less chances of developing stable angina.

Diagnosis of acute coronary syndrome is made depending on high levels of cardiac biomarkers with presence of one or more of the following signs and symptoms which include

1. Symptoms of ischemia

2. Pathological q waves in electrocardiogram or elevation or depression of ST segment.

Differential diagnosis in young patients who presents with signs and symptoms of ACS should include myocarditis. Myocarditis should be suspected in all young patients who presents with ACS signs and symptoms but normal coronary arteries proven by coronary angiogram[92, 93].

NON-ST ELEVATION MI

These patients with non-ST elevation (non-Q wave) MI or unstable angina) are initially stabilized using medical treatment, followed by

revascularisation after early coronary angiography. These patients can be risk stratified based on exercise stress test.

Wolfe MW et al did a study on MI patients with age less than 35 years and re that exercise testing in asymptomatic young patients after myocardial infarction helps in identifying individuals coming under minimal risk category. In this study almost 19 subjects had minimal lesion in angiography done for assessing prognosis and each of them underwent exercise stress testing in which most of them reached up to stage four[75].

It is recommended that early coronary angiography is indicated only for those young patients with features suggestive of high risk category i.e. multiple risk factors or ischemia that is recurrent.

COMMON ANGIOGRAPHIC FINDINGS IN YOUNGER INDIVIDUALS

Young and older individuals not only differ in their clinical presentation but also in their angiographic findings. This was reported in the CASS trial that compared findings from a group of young men and women who underwent angiography (who presented with features of MI) with that of the older individuals. This was considered as one of the largest reported angiographic findings in younger individuals. Most

young patients showed higher incidence of normal coronary angiogram, minimal luminal irregularity, they are more prone to develop single vessel disease [93]. The inference of the study was

1. Normal coronary angiogram were commonly seen in young patients (especially young women)

2. Single vessel disease was more common than triple vessel disease,

3. Left anterior descending artery was more commonly affected in younger individuals[94].

There is another entity called spontaneous coronary artery dissection. This spontaneous coronary dissection though rare should be considered in younger patients who present with features of acute coronary artery syndrome (especially those below 50 years of age). This is important because women are more prone for spontaneous coronary artery dissection especially in the peripartum period.

MANAGEMENT OF ACUTE MI

Management is mainly based on whether it is an ST-elevation or non-ST elevation MI. Reperfusion with the help of primary percutaneous intervention or thrombolysis and revascularization is the ideal form of treatment in younger subjects presenting with ST-elevation MI.

Studies showed better outcome with primary percutaneous intervention than thrombolysis (GUSTO-IIb trial)[95].

PERCUTANEOUS CORONARY INTERVENTION

In a study carried out by Mehan et al regarding the outcome of patients who underwent angiogram and percutaneous interventions the ten year event free and survival overall was 58% and 96% in the age group of less than 40 years i.e. good outcome[97, 98].

Restenosis and disease progression can be prevented by stenting of coronary arteries, particularly with drug-eluting stents and anti-platelet therapy and with lipid lowering drugs.

CORONARY BYPASS SURGERY

In a study carried out by Vedder et al regarding revascularisation procedure done on CAD patients and the outcome in such patients, he found that the it was better tolerated in younger than older individuals because of better physical condition and tendency to withstand anaesthesia and had better survival rate i.e. 93% and 81%, 72 percent and 57 percent after 5 and 10 years post surgery. Factors like number of vessels involved, ventricular function, smoking, coronary artery disease in family influence the outcome[99].

The patency of the graft was better with mammary artery than compared with saphenous vein graft i.e. it was 93% with mammary and 56% with saphenous vein graft. Arterial grafts were preferred over venous graft because of good patency.

PROGNOSIS AFTER MI

Young patients with acute coronary syndrome are potential candidates to develop adverse outcome in terms of prognosis, but severe coronary artery disease was uncommon and had documented good prognosis both on short and long term basis[96].But mortality in hospital was zero to four percent less than older individuals.

LONG-TERM OUTCOME

Survival rate for young men was 84% compared to 75% in older men after 7 years of myocardial infarction, whereas it was 90% for young women and 77% older women.

Recurrent infarctions and mortality risks were documented in patients less than 45 years of ages who were followed up after acute myocardial infarction for 6 to 9 years period, and the event rate was found to be around 50 % which include coronary revascularisation, acute myocardial infarction and death.

Secondary preventive measures like intensive efforts to reduce risk factor should be appropriately initiated which includes cessation of smoking, physical exercise program, management of obesity and depression, diabetes and hypertension.

CORONARY CARE UNITS

Till 1961subjects who presented with AMI were admitted in the hospital in a separate room remote from the nursing station to assure adequate rest to the patients. But a lot of the times patient were found dead in their beds. Almost 30 % of patients who got admitted with AMI were found dead due to possible arrhythmia[108].This led the physicians to establish CCU for all time monitoring of patients through ECG,along with defibrillators and other resuscitation measures. This resulted in 50 % reduction in CVD mortality in hospital admitted patients with MI.

INVASIVE CARDIOLOGY

William Harvey in the year 1628 was the first to describe cardiac function and coronary circulation[109.] This gave the physiologist from France C.Bernard the idea to catheterize animals. He measured aortic pressure and pressure in the heart chambers[110]. W.Forrsmanin the year 1929 tried catheterising himself and this was the first experimental catheterisation done in humans. This was followed by study on

hemodynamic of the heart by the two physicians AF Cournand and WW Richards[111]. C.Bernard, Werner Frosman Cournand and WW Richards all were given Nobel Prize in the year 1956 for their contribution in the field of medicine[112.] In 1958 this along with ventriculography became a valuable tool to assess the coronary artery anatomy and ventricular function [113].This was followed by exploration of heart through surgical techniques for revascularisation[114].Though A Gruntzig was called as the father of PCI, the contribution done by Dotter and Judkins in the field of invasive cardiology was remarkable. In the current set up DES (drug eluting stents) are more commonly used rather than routine BMS (bare metal stents) to prevent restenosis115.

NEWER MODALITIES OF TREATMENT

In the year 1970 the mortality of patients admitted in the hospital for MI the one year after discharge was studied and it was found to be around 15 percent. Among them 10 percent deaths were due to heart failure secondary to large size of the infarct. In a study done on animals it was found that the size of the infarct can be decreased altering myocardial oxygen demand and oxygen supply[116]. Fibrinolytics came in to existence in the year1976and were found to lyse the clot in acute MI patients they were given as an infusion in to the heart[117]. In the GISSI study which included about ten thousand subjects the efficacy of streptokinase

infusion intravenously in reducing CVD mortality in AMI was confirmed[118]. This study was followed by ISIS-2 study in which antiplatelets like aspirin along with the fibrinolytic agent were found to decrease death in CVD patients further[119]. The mortality rate was found to be very low with newer modalities of treatment like angioplasty with stents especially drug eluting stents, newer anti-platelets and was found to be as low as 7 percent[120]. All these modalities of treatment have added advantage only when patient present early to the hospital after initiation of symptoms[121].

SAVE, a randomised control trial suggested long duration of treatment with ACEI in patient with MI with LVD (left ventricular dysfunction) as it was proven to decrease the mortality in these patients[122].

Usage of β-blockers, aldosterone antagonist was found to have remodelling effect on infarcted myocardium and has reduced the mortality in MI patients further. But even then the possibility of developing severe LVD when patient develops large infarction secondary to excessive scarring of the ventricle exixts. The mortality in these patients can be reduced by ID[123] (implantable defibrillator), CRT (cardiac resynchronization therapy), pacemaker[124] and through assistive devices for ventricles[125].Heart failure patients have defect in calcium pump

SERCA 2a. In a pilot study it was found that through gene therapy using adenovirus, gene for SERCA 2a can be delivered as infusion into the coronaries to improve the function of cardiacmyocytes [126]and was found to have proven benefit.

NSTEMI / UNSTABLE ANGINA

Ischemic heart disease patients can be broadly divided in to two categories i.e. those who have coronary artery disease for long time and those who presents acutely. Those patients who present acutely may have STEMI or unstable angina/NSTEMI. STEMI/NSTEMI though appears different represents necrosis of the myocardial tissue (AMI). ST elevation in ECG with elevated cardiac biomarkers and presence of typical anginal symptoms is called as STEMI, whereas ST segment depression and T wave inversion along with raised cariac biomarkers and presence of typical anginal symptoms is called as NSTEMI. The difference is due to the size of the area infracted.They both cause release of cardiac biomarkers which helps to differentiate them from unstable angina. Hence unstable angina cannot be called as myocardial infarction. Recently ESC/ACC proposed a new definition i.e, amount of necrosis produced by ischemia can be STEMI/NSTEMI. NSTEMI and unstable angina patient needs treatment with dual anti-platelets therapy plus anticoagulant (LMWH), statins, adequate bed rest and needs continuous

monitoring as they are more prone for arrhythmias. And it was found that level of cardiac biomarker is directly proportional to the mortality and there is a definite indication to continue lipid lowering drugs[127] and anticoagulant usage in such patients[128].

SIGNIFICANCE OF MOLECULAR STUDY IN CORONARY ARTERY DISEASE

The familial risk factors of the CAD and atherosclerosis were extensively studied by genomic study[144, 145]. From these studies it was found that various chromosomes with different genes synthesising different proteins causing lipid level alterations. It was also found that the inflammatory process involved in the development of CAD secondary to atherosclerosis was due to the link between SNP's with chemokines. Hence the knowledge on molecular targeting became essential[145].

For drug dosage and selection the pharmaco-genomics which gives us the information about genetic difference in the response to drugs in different patients is essential. Fourty percent of the patient receiving same warfarin dose in a study, showed variation in two genes which codes for the liver metabolism of warfarin. Similarly clopidogrel showed less efficacy due to variation in cytochrome genes, increasing the mortality in these patients and there is also a increased risk of developing CAD[146].

Numerous clinical trials using progenitor cells to repair the myocardial insult are on and results are awaited [147-149]. It was also found that tendency of the stem cells to migrate inside the body in response to various paracrine signals has received much attention because this can be used to rejuvenate injured cardiac tissue[150].

BURDEN OF NON-COMMUNICABLE DISEASE

The global incidence of CAD is evolving slowly that it is varying widely among different age, gender and social quality of life among different societies. This is evident by the increasing occurrences of CAD in under developed countries . In a study done by WHO in the year 2002 it was found that non-communicable disease accounted for 32 million deaths worldwide, which was nearly three fourth of the global death rate. For instance, south East Asia in 2002 had nearly 7,413,100 deaths due to non-communicable disease.

It thus the major mortality factor worldwide except in Africa. So overall IHD was found to be the leading cause of mortality in subjects aged greater than or equal to 60 and it stands second only to HIV in the younger group aged below 60 years[151, 152]. The increased expectancy of life among Indians has made prevalence of CVD to rise, as the disease process starts producing manifestation more commonly at the later ages of life.

CARDIOVASCULAR DISEASE IN INDIA

In the past few decades the risk of developing CVD in India seems increasing compared to foreign nations[153]. Various studies conducted on Indians residing in different nations showed Indians have more than 3 times higher risk of developing atherosclerotic cardiovascular disease than compared people living in America, 6 times when compared to China and 20 times when compared to people in Japan[154-15].

As there was no proper maintenance of death register in India it became difficult to assess actual burden of the disease that time[158]. Different other studies done independently in north India showed increasing trend in the distribution of CAD among rural and urban population[159, 160]. It was found from one study that the disease burden rised in urban Indian population from 1% to 10% and there was two fold increase in the mortality due to CAD in rural India compared to previous years(with south Indian rural population having highest prevalence of 7%)[169]. Also the disease burden was higher in south India than compared to north and it was 14%[161,162,163].

In rural India, a twofold increase has been reported in the northern states[164-168].The incidence keeps rising in the younger in younger individuals especially in the working age group i.e. 35-64 years which comes around 12 to 16 percent of the population[170, 171]. In India 50% of

the death due to cardiovascular disease is under the age of 50 years and 25 percent of the cases with AMI are under the age group of 40 [172] ,which was similar that of the INTERHEART study[173]. In Asia, Indians have the highest chance of developing CAD. The percentage of patients below 40 years who experience first attack was found to be 4.4 and 9.7% among Asian men and women respectively, this is twice as high as European and the third highest in the world[173].This study concluded that Indians have higher chance of developing MI even before the age of 40.

CREATE REGISTRY STUDY

In this study 20,937 patients were registered from 88 centres from various regions and cities in India[17.]. Of this 60.6% patients had STEMI .These STEMI patients were found to have an average age of 56 years, whereas in NSTEMI it was 59.3 years. They were from middle and poor socioeconomic class (52.3 and 19.6%).The average time taken to the hospitilisation from the onset of symptoms was 360mins and for the initiation of thrombolysis was 50 mins on average. Of the total patients in this registry, it was found that diabetics were 6226, hypertensives 7220 and smokers 8242.

TABLE 4: PREFERRED TREATMENT OPTIONS PRACTISED IN STEMI/NSTEMI

TREATMENT	STEMI (in %)	NSTEMI (in %)
Anti platelets	98.2	97.4
ACEI/ARB	60.5	51.2
Statins	50.8	53.9
Beta blocker	57.5	61.9
CABG[174]	1.9	4.4
PCI	8	6.7

Most of the STEMI were treated with anti- platelets, ACE inhibitors/ARB and PCI, whereas NSTEMI patients received more of Beta blockers, anti-lipidemics and CABG. The outcome was measured in terms of stroke, chances of reinfarction and death.

TABLE 5: OUTCOME IN PATIENTS WITH STEMI/NSTEMI

PARAMETERS	STEMI (in %)	NSTEMI (in %)
STROKE	0.7	0.3
REINFARCTION	2.3	1.2
DEATH	8.6	3.7

From this it is evident that NSTEMI had better prognosis than STEMI. The outcome was also determined by the social class of the patient, where 60.9% of the rich received thrombolytic but only 49.6% of the poor. Of rich 61.2% received anti-lipidemics compared to 36% of the poor. ACEI /ARB, PCI/CABG were more commonly used in the rich.

RISK FACTORS AMONG INDIANS

The main disadvantage of the previous studies on the causative factors of premature CAD was that it was mostly done with migrant population of India. As a result, the outcome of these studies cannot be generalised because a large proportion of the study sample were from same community and certain communities were either small in proportion or neglected in the study.

Indians have had cardiac illness 5 to 10 yrs earlier than the rest of the world[179, 180].

From the INTERHEART STUDY[22], it was found that the South Asians have 53 years as the average age of onset of the acute Myocardial Infarction when compared to the western countries the mean age was only 63 years, with more incidence among men. From this study it was evident that the onset of initial symptom of MI among Asian women was 58 years whereas it was 54 years among the Asian men. Even though Asian women have delayed age of onset of the disease, they have poor prognosis than Asian men[181-185]. The reason for this increased mortality due to MI among young Asian women is not clear.

The INTERHEART study[173] which involved 52 countries established a significant co-relation between various modifiable causative factors among different regions, sex and ages. The Apo protein B / Apo protein A1 and smoking had an odd ratio of 3.81 and 2.43 were found to be the major causative factors among South Asians. Worldwide the psychological factors had an odds ratio of 2.67 whereas in South Asia it was only 2.15, but the HTN, truncal obesity and DM had greater odds ratio of 2.89, 2.43, and 2.48 respectively among young Asians. It was also found from the INTERHEART STUDY[173], young women with DM and increased blood pressure had higher risk of developing CAD than young men in India.

The Jaipur Heart Study-2 showed a significant relation between smoking, sedentary lifestyle, deranged lipid profile, increased blood pressure and abdominal adiposity and CAD among the young men and women of Jaipur[186]. There was also considerable increase in the existence of abdominal adiposity, DM and deranged lipid profile in the same population when compared with the old Jaipur Heart Study conducted at 1990. It became evident from various studies that upper socioeconomic class population had increased existence of DM and increased blood pressure when compared to the lower class population in Chennai city[187].

There was wide variation in the lipid range among the CAD population in North and South India when compared with the non CAD population. The population from Northern part of India had prevalence of CAD at lower levels of cholesterol and there was a greater correlation between total cholesterol and LDL in CAD prone young population of India (less than 40 years of age). Low HDL-C and high triglyceride levels were the major causative factors among both young and old population of India[195, 196]. The major attributable risk factor in the Indian population was deranged APO B / APO A1 levels in both men and women. Many studies showed that young males of India had lower existence of HTN and DM than the young women population of India[189, 190].

Sedentary lifestyle and smoking were more common among urban population of 20 to 39 years of age in India [186].

From the INTERHEART study[173,] it was also evident that smoking was a major causative factor among the younger men in India, thereby increasing the risk of coronary artery disease among this population. It became evident that there is no safe range for smoking by comparing the OR of smokers (>40 cigarettes/day) which was 9.16 to those of non-smokers it was only 1.38. Many other Indian studies also found that greater correlation existed between smoking and CAD among young Indian population[191, 194]. It has been found that there is a higher existence of smoking, about 44.6 percent in south Indian men and 45.3 percent passive smoking in south Indian women than the northern population of India[161]. On the contrary the rural population of India did not have smoking as major causative factor for acute myocardial infarction, but they had increased blood sugar levels and their waist: hip ratio was normal[197]. Positive family history for CAD became a significant causative factor for CAD among young Indian population [188-191].

From INTERHEART study[173,] positive family history was significantly higher among the younger CAD patients with a PAR (Population Attributable Risk) of 14.8 % to only 10.45% among older population. When compared to other causative factors the contribution

attributed by positive family history for development of CAD is only by 1%. But it should be kept in mind that various other correctable causative factors for CAD (like cholesterol levels, obesity etc) were also determined genetically to some extent. The genetic study became significant as familial CAD occurrence emerged in as the second major causative factor for CAD among young population in India [194].

DIABETES MELLITUS AND CAD

Diabetes mellitus is characterised by insufficient production of insulin or by the failure to respond appropriately to insulin, resulting in hyperglycaemia. The diagnostic criteria are summarized in Table 1. Importantly, new to the diagnostic criteria in glycosylated haemoglobin (A1C) level > 6.5% has been added. Type 2 diabetes , characterised by relative insulin deficiency with the backdrop of insulin resistance and representing >90% of all diabetes cases. Type 1 diabetes is characterised by absolute insulin deficiency.

Diabetes is among the most common chronic diseases in the world, affecting an estimated 180 million people in 2008[199]. Confounding this high global burden is the increasing incidence and prevalence of type 2 diabetes, driven by increasing population age, obesity and physical activity as well as by the increasing longevity of patients with diabetes.

Estimates project that more than 360 million persons will be affected by diabetes by 2030.

Table 6: American diabetes association criteria for diagnosis of DM[198]

Fasting blood sugar >126 mg/dl Or 2 hour post prandial blood sugar >220mg/dl with 75-g oral glucose tolerance test Or Symptoms of hyperglycemia plus nonfasting plasma glucose >11.1 mmol/liter(>200mg/dl) Or HbA1c >6.5%

Previously much attention was given to prevent micro vascular complications this led to the shift in trend towards development of macro vessel complications related to coronary vessel, peripheral vessel and cerebral vessels. This emphasis on to look for cardiovascular disease risk especially in people with DM as it can cause major public health problem.

Comparing with non diabetic individuals, patients with diabetes have a 2-4 times increased risk for development and dying of CHD[200]. Previous studies showed that there were no significant difference in the risk of development of cardiovascular disease in relation to whether patient was a diabetic or non diabetic (pertaining to MI), that is, a "coronary disease equivalent", more recent observations from clinical trials suggests a substantially lower CHD risk, most likely reflecting the effectiveness of contemporary therapeutic interventions[201-203]. Diabetes is associated with an increasing risk for MI. Across the spectrum of ACS events, in which diabetes , may affect more than one third of patients,[204] patients with diabetes have worse CVD outcomes.[205] Despite overall improvements in outcomes during the past several decades for ACS, the gradient of risk associated with diabetes persists.[205]Furthermore, the increased risk observed with the diabetes in the setting of ACS events extends to glucose values in the range well below the diabetes threshold, whether it is analysed by glucose values at the times of presentation or those observed throughout hospitalisation.[206]

Diabetic individuals are more prone for developing complications secondary to atherosclerosis which has its impact on outcome independent of primary and secondary prevention strategy.

PREDIABETES AND CAD

Most of the American citizens around 36 million were found to have intolerance to glucose, this when combined with obesity will result in development of overt diabetes, resistance to insulin and cardiovascular disease over a period of time[207].CVD risk started to rise even before the development of overt diabetes, this was proved in a study called the Nurse health study which showed that the late onset diabetics were shown to have 3 fold risk of developing MI even before establishing diagnosis of overt diabetes which is equivalent to those who already have diabetes for long time i.e. in overt diabetes at the entry of the study[208].

Although hyperglycemia associates with vascular complications, resistance to insulin alone can increase development of atherosclerosis before the patient develop overt diabetes and the available data also proves this. All this made health professionals to search for MS components in individuals at high risk of developing CVD.

TABLE.7: MECHANISM IMPLICATED IN DIABETIC VASCULAR DISEASE

Endothelium	↑ NF-kβ activation ↓Nitric oxide production ↓ Prostacyclin bioavailability ↑ Endothelin 1 activity ↑Angiotensin II activity ↑cyclooxygenase 2 activity ↑ Thromboxane A2 activity ↑Reactive oxygen species ↑ Lipid peroxidation products ↓ Endothelium-dependent relaxation ↑ RAGE expression
Vascular smooth muscle cells and vascular matrix	↑Proliferation and migration into intima ↑Increased matrix degradation Altered matrix components
Inflammation	↑ IL-1β,IL-6,CD36,MCP-1 ↑ICAMs, VCAMs, and selectins ↑Activity of protein kinase C ↑ AGEs and AGE/RAGE

AGEs- advanced glycation end products; ICAMs-intracellular adhesion molecules; IL-interleukin ; MCP- monocyte chemo attractant

protein; NF-nuclear factor; RAGE- receptor for advance glycation end products; VCAMs-vascular cell adhesion molecules.

Elevated glucose level has its role in development of atheroma directly by increasing the following parameters in the blood

1. FFA (Free Fatty Acids)

2. Advanced end products of glycation

3. Inflammation of vascular system

4. Endothelial dysfunction

All these speed up the process of developing atheromatous plaque and its rupture.

In addition, the pernicious effect of hypoglycaemia complicating diabetes therapy, the sympathovagal imbalance due to diabetic autonomic neuropathy, and vascular effects of exposure to excess insulin may contribute to atherosclerotic risk.

Endothelial dysfunction, a hallmark of diabetic vascular disease, is associated with increased hypertension and adverse CVD outcomes. The myriad mechanism contributing to endothelial dysfunction include abnormal nitric oxide biology and angiotensin II, and reduced prostacyclin activity, all of which contribute to abnormal control of blood flow. In the setting of ACS events, no reflow after percutaneous

intervention reflecting acute endothelial dysfunction occurs more commonly in the presence of diabetes or hyperglycemia and may contribute to increased myocardial jeopardy, resulting in larger infarcts, increased arrhythmia, and worse systolic function.

Diabetic dyslipidemia is characterised by high triglyceride levels, low HDL and increased atherogenic small dense LDL particles, each of which is likely to contribute to the accelerated development and progression of atherosclerosis. Perturbations in the fibrinolytic system and platelet biology further compound the direct vascular effect of diabetes, yielding a constitutive prothrombotic milieu. These abnormalities include increased circulating tissue factor, factor VII, Von Willebrand factor, plasminogen activation inhibitor 1, with decreased levels of anti-thrombin III and protein C. In addition, disturbances of platelet activation, aggregation, morphology and life span further contribute to increased thrombotic potential, as well as to the acceleration of atherosclerosis.

TABLE 8: ABNORMALITIES OF PLATELET FUNCTION ASSOCIATED WITH DIABETES

Reduced membrane fluidity
Altered ca^{2+} and Mg^{2+} homeostasis
Increases 1. Arachidonic acid metabolism 2. Thromboxane A2 synthesis 3. Oxidation of free radicals 4. Adhesion molecule expression on cell surface of endothelium like glycoprotein IIb/IIIa which help in adhesion of platelets.
Decreases 1. Nitric oxide synthesis 2. Synthesis of prostacyclins
Increased platelet micro particle formation
Increased platelet turnover

Increased systemic inflammation secondary to poor glycemic control increases the possibility of developing overt diabetes and diabetic atherosclerotic disease, this together with oxidative stress and deposition of end products of glycation aggravates the progression of the whole

disease process , yielding plaques with characteristics of higher risk in both coronary and carotid arteries.

PREDIABETES AND CAD –EVIDENCE

A meta-analysis[209] with regards to relative risk,the development of CVD in patients with impaired glucose tolerance ranges up to 1.30 and with impaired fasting glucose it is 1.37. This risk increases proportionately with increase in fasting blood glucose from 100 to 110 mg/dl. This differs between men and women.

However there is no significant data available on patients with impaired glucose tolerance or impaired fasting glucose levels in the recent past. This is attributed to the fact that previous studies used WHO criteria that says fasting blood sugar greater than 140 and two hour post prandial blood sugar between 140 to 200 was considered significant. However they found that 2 – fold increase in the CVD risk in the patients studied.

A study was carried out in the year 2001,called the DECODE study which says that there were no significant difference between male and female with respect to relative risk of developing CVD in IGT patients[210.]

The possibility of developing CVD in patients with pre-diabetes if they did not progress to overt diabetes in not clearly known [or] studied[211].

It is also difficult to screen individuals with regards to prediabetes. Some studies support screening patients with prediabetes and others do not. American diabetic association says it is important to screen prediabetic patients who are at risk of developing CVD or overt diabetes based on the knowledge of WC/BMI/age etc

In summary the burden of the CVD risk in prediabetic remains unclear. People like Americans, Indians are at increased risk of developing diabetes and they recommend regular screening for development of CVD and diabetes in these individuals..

PRE-DIABETES IN INDIA

In Asians especially south Asians MS is more prevalent, this is due to the fact that south Asians have increased body fat with metabolic abnormalities at low WC or BMI. Criteria that we routinely use when applied on these patient may result in spuriously lower prevalence or distribution of MS. To overcome this SAM-NCEP developed a criteria which has suggested to keep abdominal adiposity component as an optional one. But IDA (International Diabetic Federation) has suggested ethnic and race specific cut-off to avoid under estimation of actual distribution of MS in the community.

The risk for developing CVD in Asian Indians is 2-fold higher when compared to other foreign nations. This is attributed to high

prevalence of hypertriglyceridemia and low HDL cholesterol levels in blood. Hence Asians especially south Asians have high chance of developing CVD which needs active intervention by life style and behavioural modification starting early in life.

PHENOTYPIC VARIATION IN ASIANS

Asians, especially Asian Indians though phenotypically donot look obese, their metabolic parameters appears deranged most of the times[212]. Hence they cannot be considered normal even when their BMI falls less than 25.

Compared to India western countries have only 6% of population comprising the above mentioned phenotype[213]. This is attributed to certain features which are unique to Indian population. These includes

1. High degree of lipid derangement
2. Decreased adiponectin levels
3. Hips are thinner but have increased waist circumference
4. Legs are short
5. Increased fat deposition in the viscera

All these factors predisposes to increased risk of developing CVD and DM[214].

Increased fat deposition in viscera which is disproportionate to the corresponding waist circumference makes them more prone to develop

resistance to insulin.This is commonly seen starting from the age as earlier as eight years[215].

Children in India have higher insulin levels compared to their counter parts in other nations with relation to waist circumference. All the above mentioned factors together with higher concentration of PAI-1 levels and fibrinogen levels in South Asian population makes them more prone to develop CVD and DM[216].

DIFFERING CRITERIAS IN ASIANS

Because of the above mentioned observations, the following difference has been made in the criteria's previously established

1. In WHO –for Asians they have decreased the BMI cut offs has been declared or more 23 in the overweight category and more than 25 for obese individuals[217]. Based on the above change in the criteria, UKDAS[218] study was carried out. In the study they found that most DM patients belong to the category of overweight and obese which is around 95% and 80% in South Asia respectively. It was also suggested that usage of waist circumference cut-off of 87 cms and 82 cms for males and females could definitely help in identifying correctly the individuals at risk of developing DM and CVD in Asian Indians dwelling in urban areas[219].

2. The IDF proposed the waist circumference cut off to be 90 and 80 cms for men and women dwelling in South east Asia[220].

3. AHA/NHLBI in the year 2005 has reduced the waist circumference cut-off for Asians living in America to less than 90cms and 80 cms for men and women[221].

4. The South Asians modified (SAM) NCEP guidelines is almost the same as IDF criteria but the exception is abdominal adiposity which was not considered as a principal component but was kept optional[221-222].

When applied to the study population an increase in the prevalence of obesity from 25 percent to 50 percent was found

Thus MS is more prevalent in south Asians than compared to Europeans and other Asians. Implementing primary and secondary prevention strategies becomes essential to control the prevalence of DM and CVD related morbidity and mortality. Hence weight reduction, regular exercises, and low fat/ anti atherogenic diet starting from childhood years is vital to stop further progression of this metabolic abnormality to become overt diabetes and CVD.

Consensus statement for revised cut-off for abdominal obesity in Asian Indians:

Methodologies of WC measurements are as follows:

With the patient standing, using a flexible tape at a point above iliac crest, ideally in the empty stomach, and during expiration waist circumference should be measured.

For measuring abdominal adiposity most study recommend the usage of waist circumference as more reliable than measuring WHR that too especially in Asians as ethnic and race specific cut-offs are available.

Table 9: WAIST CUT-OFFS AND SUGGESTIONS

WC in Asians(in cms)	Suggestions
78 for male and 72 for female	WC higher than the mentioned values are suggested not to gain weight. Physical exercises are advised.
90 for men and 80 for women	Advised to seek help from medical professionals for reducing weight. To be investigated and managed for other related risks

There are inherent difficulties in obtaining hip circumference accurately in community settings. Furthermore, changes in WHR may not reflect changes in adiposity accurately and the ratio may be normal in generalised or gynaecoid obesity. Hence the consensus group opined that it may not be used routinely as a measure of abdominal obesity.

VITAMIN D AND METABOLIC SYNDROME:

Metabolic syndrome is characterized by hypertension, hyperlipidemia , and insulin resistance , with or without obesity, all of which have been linked to vitamin D nutrition (VDN). Vitamin-D deficiency is more commonly seen in patients with metabolic syndrome, but it is unclear that whether this is a cause or a consequence of the associated obesity. Patients with low levels of 1,25-dihydroxy vitaminD3 were found to have high levels of VLDL and hypertriglyceridemia. This may be attributed to the development of resistance to insulin action in patients with deficiency of Vitamin D and this finally results in MS[223.] This relationship with vitamin D deficiency was established both in experimental animals and in human observational studies[224,225] The proposed mechanism for developing diabetes- like state in subjects with vitamin D deficiency include

1. Altered calcium homeostasis in β-cells of the pancreas

2. Altered expression of insulin receptors on the cell surface

3. Development chronic inflammatory state[225,226]

4. Decreased expression of insulin receptor on the cell surface leads to insulin resistance thereby developing a pseudo diabetic state.

5. Transport of glucose in to the cells were also disturbed in the back ground of vitamin-D deficiency[229,230].

This was evaluated by studies done on animal models which showed decreased secretion of insulin after ingestion of glucose, though its basal level of insulin remain unaltered in a vitamin D receptor knocked out mouse[226-228].

It was found in many studies that deficiency of vitamin-D was more common in subjects with type 2 diabetes mellitus, gestational diabetes, and in patients with impaired glucose tolerance.

In a prospective European Society Study on diabetes prevention (EURODIAB[231]) it was found that more than 30 percent decrease in the incidence of developing DM in children after supplementation of active form of vitamin-D.

MICROALBUMINURIA AND VASCULAR ABNORMALITIES

Microalbuminuria has significant influence on vascular system. Several cross sectional studies found that microalbuminuria is associated with higher thickness of the intima and media layers of the carotid artery. Moreover in a study by Bruneck, a prospective population based survey of 683 Caucasians adults, showed albumin creatinine ratio has direct and independent relation with severity of atherosclerosis of femoral and carotid artery. Moreover increased levels of albumin creatinine ratio are associated with silent cerebrovascular disease (silent cerebral infarcts and brain micro bleeds). Microalbuminuria also predicts the development and progression of carotid atherosclerosis. Hypertensive patients with microalbuminuria were more prone to retinal vascular changes. Individuals with urine albumin excretion ≥20μg/min had a prevalence of hypertensive retinopathy of 69%, significantly higher than that observed in subjects with urine albumin excretion ≤11 μg/min.

In the large Netherland cohort study in the name of PREVEND found that there is a significant relationship exist between albuminuria and CVD i.e. increased excretion of albumin in the urine will result in 28 percent raise in the mortality secondary to cardiovascular disease cardiovascular diseases and there was a continued association between cardiovascular disease and albminuria. Data from NHANES –III study,

spanning a thirteen years follow-up of 14586 adults revealed a two fold increase in albumin levels in the urine resulted in 6.3 percent raise in death related to CVD and the same 6.3 percent raise in death rate pertaining to all other cause, adjusting other predictable risk factors. It was also found that there were no significant differences in the death rate pertaining to albuminuria in diabetic and non diabetic population involved in the study.

MICROALBUMINURIA AS PREDICTOR OF CARDIOVASCULAR MORTALITY AND MORBIDITY

A meta analysis evaluating a relation between microalbuminuria and mortality in Type 2 diabetes found that microalbuminuria doubled cardiovascular morbidity and more than doubled the all-cause mortality rate. Recently, these results were confirmed in HOPE study which revealed albumin in urine has direct relation to CVD progression. It provides the information that the disease process will start to progress even at the albumin level of 4.4mg/gm in the urine. Similar analogous results relating urine albumin excretion to cardiovascular risk has been shown in Copenhagen Heart Study and LIFE trials.

Studies like PREVEND, HOORN study, DANISH-MONICA, the study Earle et al, showed the strong association of urine albumin

excretion with ischemic heart diseases, silent myocardial MI, and resting ECG abnormalities.

Studies like EPIC- Norfolk, Shibata study, Portland study, associated strongly, urine albumin excretion to strokes and recurrent strokes. Finally cross sectional studies like Zerden et al showed urine albumin excretion's close association with peripheral arterial disease.

TREATMENT OF MICROALBUMINURIA

Clinical trials showed proven benefit of using angiotensin converting enzyme inhibitors in controlling excretion of albumin in urine that too especially in diabetics.

ARB's were also found to have similar role like that of ACEI in controlling protein excretion in urine.

GAG and Diuretics like thiazides was also found to be beneficial in this aspect.

Reduced salt intake, adequate blood sugar control helps preventing microalbuminuria thereby preventing overt protein excretion and diabetic nephropathy.

Adequate control of CVD, metabolic disease control can be established by identification of development of microalbuminuria in

patients by implementing life style management and control of other causative factors[232-234]

METABOLIC SYNDROME AND LV DYSFUNCTION

Numerous studies conducted on patients with MS revealed the presence of diastolic dysfunction more common than systolic dysfunction. Patient with MS were found to have decreased E/A ratio and the number of criteria has a direct relationship i.e the more number of MS features present in a subject the more likely is the chance of developing worsening diastolic function.

Many were found to have normal ejection fraction with poor diastolic function called by HFNEF (Heart Failure with Normal Ejection Fraction). All the above findings were confirmed individually through following studies Lisa[235] et al, H Masugata[236] et al, and Azevedo[237] A, et al.

MS-PAST/PRESENT/ FUTURE

Primitive man developed a the features that go to make the metabolic syndrome (MS) in the body to withstand periods of starvation and drought. Those who inherited the genes for MS survived by storing energy in the form of fat so that during periods of famine sufficient energy to survive was available. Fifty percent of the MS is due to genetics

and /or the uterine environment. During critical periods of intrauterine development, in the process of survival and to conserve energy to the growing foetus, the foetus becomes resistant to the action of insulin. Although later in life this in-utero acquired insulin resistance, may help protect against starvation, in the modern day environment their is excessive availability and utilization of calories, fats and carbohydrates. This resistance to the action of insulin becomes pathological. This is particularly true if following the birth of a small baby 'catch up' growth occurs. The finding that the intrauterine environment , through genetic imprinting is more important than the true genetics of the foetus, comes from the recent observation of the children born to the mothers who have previously lost weight through bariatric surgery are less resistance to the action of insulin than are those born at the time of the previous greater maternal obesity. Birth weight is one of the important deciding factors that determine the chance getting MS in the future.

Initially MS was found to be associated with diabetes mellitus, and later with cardiovascular disease. But now it acts as an independent factor which even in the absence of DM,which forms a predilection to develop cardiovascular disease, stroke, and all cause mortality. In recent times we find there is no shortage of calories but shortage of burning of the same – physical activity. The plentiful supply of inexpensive yet luxuriously

caloric food with high saturated fat content, soft drinks and syrup containing fructose are probably the forerunners of obesity predominantly abdominal. Increased life expectancy, (ageing population) is also responsible for the exacerbation of metabolic syndrome and hence prevalence of T2DM and CVD. Thus MS which provided a survival advantage in our ancestors, has now become a health hazard in current day life scenario full of stress, high caloric diet and sedentary living.

The future of MS, DM and CVD may in all probability merge into each other and modify our basic understanding of these disorders that are probably based on a‘common soil’. Despite all odds, from a clinical point of view, the cluster concept becomes very useful and advantageous in diagnosing and treating the various manifestations and complications. IR with endogenous hyperinsulinemia, large vessel atherosclerosis, pre diabetes and T2DM – all may be considered as evolving from one another, sometimes preceding and sometimes following each other. The main measureable components of MS are central obesity, dysglycemia, hypertension and dyslipidemia. These components may need refining and redefining in the near future and the years to come. For instance, the Insulin clamp study gives us data of fasting triglyceride to HDL ratio to correlate well with the criteria of diagnosing MS. Ratio exceeding 3.5 is more likely to be MS. Through genetic and environmental factors, excess

peritoneal fat infiltrated with macrophages produces excessive FFAs and harmful adipocytokines and decreased production of proactive adipocytokines – adiponectin. The net effect of this imbalance of adipocytokines is inflammation, oxidative stress, endothelial dysfunction, insulin sensitivity, excess coagulation, atherosclerosis, T2DM and adverse cardiovascular events.

To the emerging question if there are factors that help to improve the manifestations of MS, the response is predictable. Regular exercise and dietary strategies to reduce the post prandial spikes in glucose and TGs, to reduce the inflammation, oxidative stress and chronic degenerative diseases. Dietary advice should emphasise on low glycemic index foods which mimic the Mediterranean diet. Low fat dairy products, tea, coffee, olive oil, cinnamon and moderate alcohol particularly red wine intake – may improve the MS and prevent progression to T2DM. There are few drugs which may improve the various components of metabolic syndrome. However most physicians lay emphasis on dietary and exercise measures to prevent or reverse obesity and IR.

METHODOLOGY

This is a cross-sectional study on young patients admitted to PSG hospital with myocardial infarction

Patients age of 45 years or less were studied as most of the studies used age group between 40 and 45 years to describe premature CAD in the young[70,238-242]. The study was conducted over a period of six months from March 2014-August 2014. All patients admitted with Acute Coronary Syndrome (ACS), both STEMI/NSTEMI and Unstable Angina as per standard definition during this period were included in the study after consent. The study was conducted in the PSG hospital, the teaching affiliate of PSG institute of Medical Sciences and Research (PSG IMS & R) which is a teaching and tertiary care referral hospital located in the city of Coimbatore, Tamil Nadu.

The patient who did not get the complete evaluation including coronary angiogram for various reasons were excluded from the study.

The purpose of this study was explained to patients and relatives and consent was obtained. The study was approved by Human Ethics Committee of the institution before commencement.

INCLUSION CRITERIA

1. Patient with evidence of coronary artery disease proven by coronary angiogram
2. Age 45 years or less
3. Both sexes were included

EXCLUSION CRITERIA

1. The patient who did not undergo coronary angiogram for various reasons.
2. Age more than 45 years

All patients with coronary artery disease including STEMI/NSTEMI/Unstable angina were included in the study.

Patients with signs and symptoms suggestive of MI (as described by European Society of Cardiology-Joint Committee) were subjected to coronary angiogram.

CRITERIA FOR DIAGNOSIS OF MS

The IDF criteria for diagnosis of metabolic syndrome (MS) were used. This definition identifies metabolic syndrome with abdominal obesity as principle component with any two or more of the incoming variables

1. Fasting hypertriglyceridemia (mg/dl) >150 or any medications for the same.
2. Decreased high density lipoprotein cholesterol value (in mg/dl) <40 in men and <50 in women or any medications for same.
3. Elevated Blood pressure >130/85mmHg or any medications for SHT.
4. Increased fasting plasma glucose (in mg/dl) ≥100 mg/dl or previously known to have medications for diabetes mellitus

Detailed history was taken including presenting symptoms, past history of diabetes/systemic hypertension /any significant history CAD in the family/ whether habituated to alcohol or smoking.

A careful physical examination was done with reference to WC (Waist Circumference) and blood pressure before discharge. About ≥3 measurements of BP at the time of entry with values greater than 130/85mmHg on an average or any medications for SHT –was considered significant.

WC was recorded according to the national health and nutritional survey[243.] With patient in the fasting state and standing, the upper border of the iliac crest was palpated and using a flexible tape during expiration waist circumference was measured.

INVESTIGATIONS

Following investigations were done for all patients.

ECG,ECHO

CARDIAC ENZYMES

FBS/FLP

CORONARY ANGIOGRAM (CAG)

The blood sample were drawn at the time of admission and the following morning (lipid profile) and at day 5 for fasting plasma glucose.[244]

Patients underwent treatment modalities like thrombolysis, Primary Percutaneous Coronary Intervention (PCI) or conservative management as feasible and required, depending on the clinical circumstances and consent from the patient. All the subjects were treated with dual anti-platelets, statins, low molecular weight heparin and other drugs as per standard protocols.

Coronary angiogram was done in all the subjects either at admission for primary PCI or electively after initial medical stabilisation with thrombolysis or conservative treatment.

STATISTICAL ANALYSIS

Data collected from the patients were initially entered in to the Microsoft excel-sheet and data analysed using SPSS (19). Pearson's chi-square was used to compare the proportions and using independent sample t test, the means were compared. A Predictive value of less than 0.05 was taken as statistically significant

RESULTS /ANALYSIS

BASED ON THE ENTRY CRITERION 90 PATIENTS WERE STUDIED

TABLE 10: DISTRIBUTION OF MS

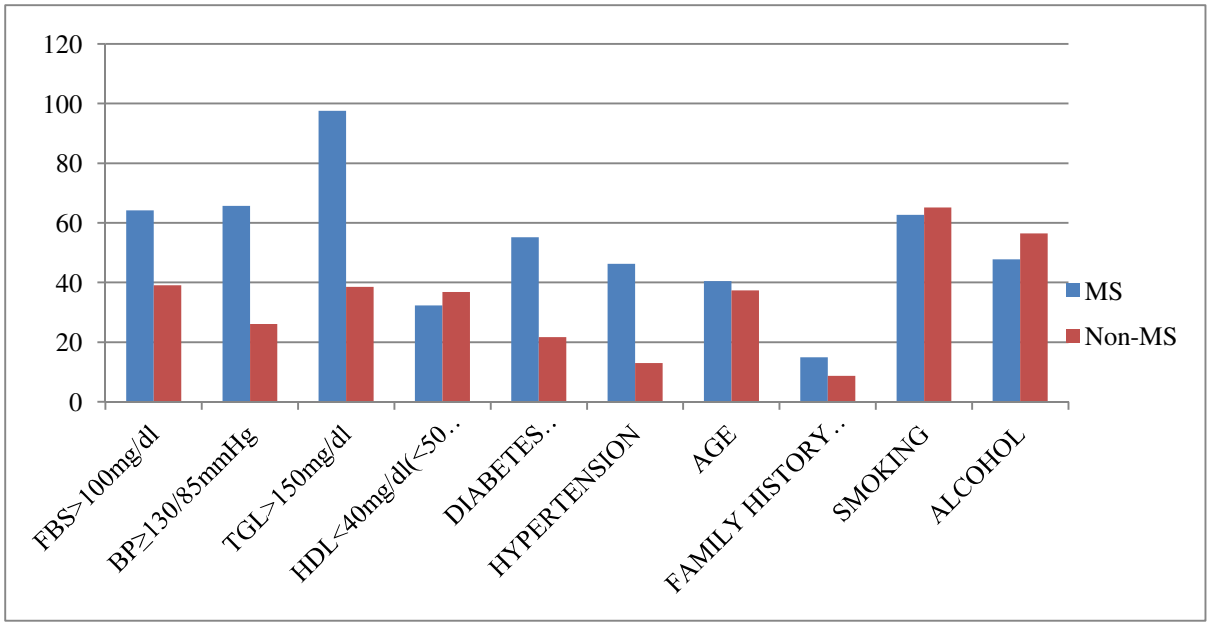
Number of CAD patients studied	**90**
Number of CAD patients with **MS**	**67 (74.44%)**

A total of 90 cases of ACS were admitted during the 6 months of study period, out of which 67 cases had MS with over all prevalence of 74.44% in the present study.

TABLE 11: BASELINE AND CLINICAL CHARACTERISTICS OF PATIENTS WITH AND WITH OUT METABOLIC SYNDROME

Variable	MS		p value
	YES (n=67)	NO (n=23)	
1.Blood pressure >130/85mmHg	44(65.67%)	6(26.08)	<0.01
2.Fasting blood glucose>100mg/dl	43(64.17%)	9(39.13%)	<0.05
3.Triglycerides (mg/dl)	179.14	115.86	<0.01
4. HDL-C (mg/dl)	32.36	36.78	<0.05
5. WC (in cms)	95.64	87.23	<0.001
6.Age	40.49	37.39	<0.01
7.Diabetes Mellitus	37(55.22%)	5(21.73%	<0.01
8.pre existing hypertension	31(46.26%)	3(13.04%)	<0.01
9.Family history of premature	10(14.92%)	2 (8.69%)	p=0.448
Coronary artery disease			
10.Smoking	42(62.68%)	15(65.21%)	p=0.825
11.Alcohol consumption	32(47.76%)	13(56.52%)	p=0.468
12.ST elevation	36(53.7%)	18(78.26%	<0.05
13. LVD	23(34.32%)	11(47.82%	p=0.24

FIGURE 3: PREVALENCE OF EACH COMPONENT IN THE IN PATIENT WITH AND WITH OUT MS



90 patients formed the study group. Of these 90 patients 67 had MS (74.44%) and 23 (25.55%) did not.

Of these 67patients with MS, 29 (43.28%) met 3 out of 5 criteria for MS, 24 (35.82%) met 4 of these 5 criteria and 14 (20.89%) met all the 5 criteria for MS.

The distribution of IDF criteria in those 67 patients diagnosed to have MS are given below

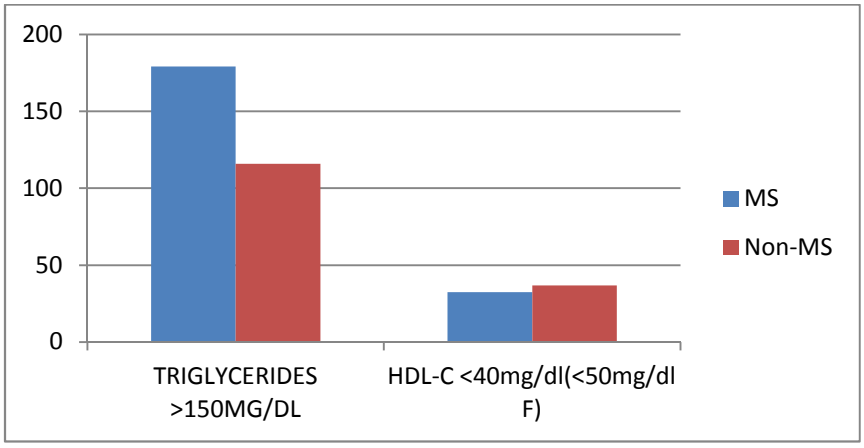
HDL-CHOLESTEROL

Patients with metabolic syndrome had an average HDL-cholesterol level of about 32.36, whereas in non-MS group the average value was 36.78 which is statistically significant.

TRIGLYCERIDES

The average triglyceride value in MS group was 179.14,whereas in non-MS group it was 115.86 which is statistically significant.

FIGURE 4: COMPARISON OF TRIGLYCERIDES AND HDL LEVELS IN MS AND NON MS PATIENTS



FASTING BLOOD GLUCOSE

Fasting blood glucose was high in 43 patients (64.17%) in MS group, whereas it was high only in 9 patients (39.13%) of the non-MS group with the p-value of <0.05 which is statistically significant.

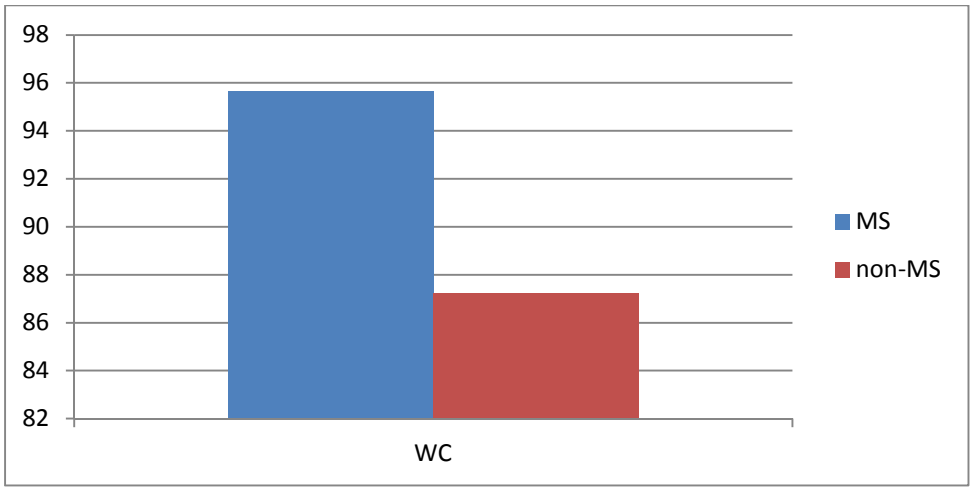
BLOOD PRESSURE

44 patients (65.67%) of the MS-group and only 6 patients (26.08%) of the non-MS group had elevated blood pressure of more than 130/85mmHg, with the p-value of <0.01 which is statistically significant.

WAIST CIRCUMFERENCE

Average WC of patients in MS group and non-MS group were 95.64 and 87.23respectively. The p-value came as <0.001 which is statistically very significant.

FIGURE 5: AVEARAGE WAIST CIRCUMFERENCE IN MS AND NON MS

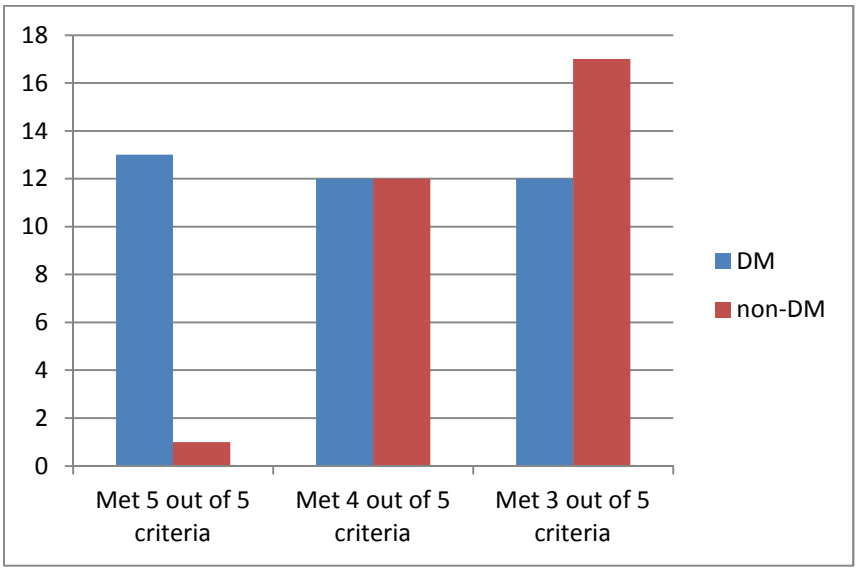


DIABETES MELLITUS

37 patients (55.22%) in MS-group and 5 patients (21.73%) in non-MS group already had diabetes and were on treatment. The p-value was <0.01 which is statistically significant.

In 67 patients with MS 14 met all the five criteria, among which 13 were diabetics. Of the 24 who met 4 criteria for MS 12 were diabetic and 12 were non-diabetic. Of the remaining 29 who met 3 out of 5 criteria for MS 12 were diabetic and 17 were non-diabetic.

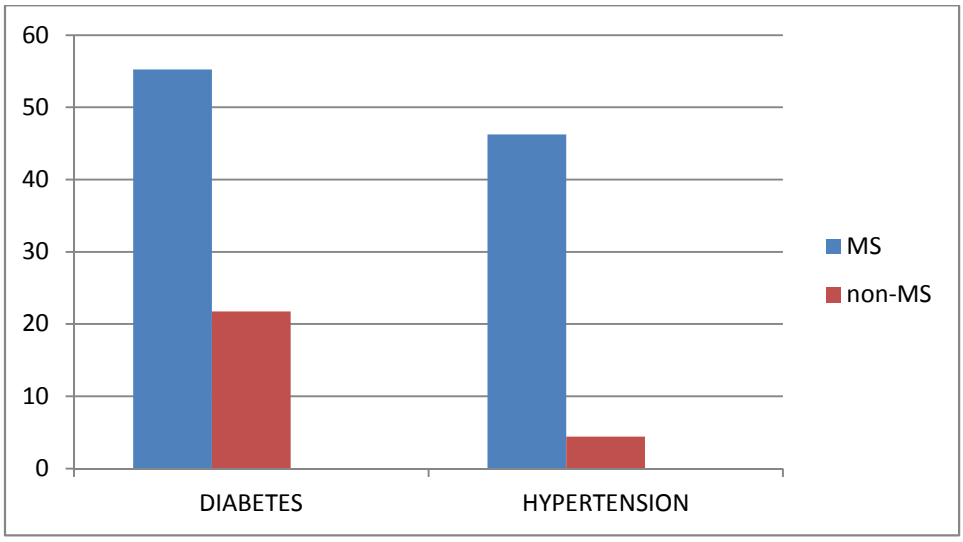
FIGURE 6: DIABETES AND MS



SYSTEMIC HYPERTENSION

31 patients (46.26%) with MS were found to have pre-existing hypertension compared to 3 (13.04%) in non-MS patients. The p-value obtained was <0.01, which is statistically significant.

FIGURE 7: PREVALENCE OF DM AND HTN IN MS AND NON MS



AGE

Average age of the patient presented with AMI in MS and non-MS group were 40.49 and 37.39 respectively. The early presentation of CAD in non-MS group may probably be due to increased prevalence of smoking and alcohol in this group.

RISK FACTORS

- **FAMILY HISTORY OF CAD**

  10 Patients (14.92%) in the MS group and 2 patients(8.69%) in the non-MS group had history suggestive of CAD in the family.

- **SMOKERS**

  42 patients (62.68%) in MS group and 15patients (65.21%) in non-MS group were smokers with p-value of 0.825(not significant)

- **ALCOHOL**

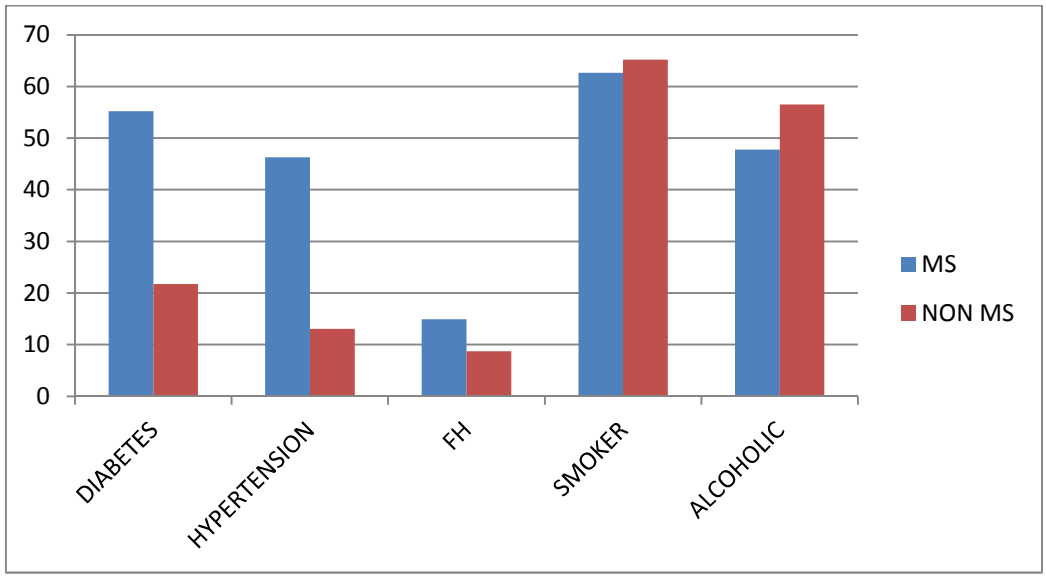
  32 patients (47.76%) in MS group and 13 patients(56.52%) in non MS group were alcoholic. p-value obtained was 0.468 which is statistically not significant.

TABLE 12 : COMPARISON OF RISKFACTORS IN MS AND NON MS

	MS		NON MS		TOTAL		P-VALUE
RISK FACTORS	NO	%	NO	%	NO	%	
DIABETES	37	55.22	5	21.73	42	46.66	<0.01 S
HYPERTENSION	31	46.26	3	13.04	34	37.77	<0.01 S
FAMILY HISTORY OF CAD	10	14.92	2	8.69	12	13.33	0.448 NS
SMOKER	42	62.68	15	65.21	57	63.33	0.825 NS
ALCOHOL CONSUMPTION	32	47.76	13	56.52	45	50	0.468 NS

S-significant, NS- Non significant

FIGURE 8: COMPARISON OF RISKFACTORS IN MS /NON- MS



ST CHANGES IN MS AND NON MS

36 (53.7%) out of 67 patients in MS group presented with ST elevation MI, whereas it is 18(78.26%) out of 23 in NON MS with the p value of 0.03 which is statistically significant (this may be attributed to occlusion of the vessel by emboli in Non-MS group but whereas in MS atherosclerotic occlusion of the vessel is more common than embolic).

LVD IN MS AND NON MS (EF <50%)

23(34.32%) out of 67 patients in MS group and 11(47.82%) out of 23 in NON MS group had LV dysfunction with the p value of 0.24, which is statistically not significant.

TABLE 13: OTHER RISKFACTORS

Other factors	MS		Non MS		Total		P value
	NO	%	NO	%	NO	%	
DYSLIPIDEMIA	15	22.3	2	8.69	17	18	0.148
HYPOTHYROID	2	2.98	0	0	2	2.2	CANNOT BE CALCULATED
ANAEMIA	1	1.49	0	0	1	1.11	CANNOT BE CALCULATED
HYPER HOMOCYSTEINEMIA	0	0	3	13.0	3	3.3	CANNOT BE CALCULATED
PVOD	1	1.49	0	0	1	1.1	CANNOT BE CALCULATED

PVOD = peripheral vessel occlusive disease

15 patients (22.38%) of MS group and 2 patients (8.69%) in non MS group had dyslipidemia and were on treatment (p value of 0.148- statistically not significant)

2 patients (2.98%) in MS group had hypothyroid and 1 patient (1.49%) in MS group had anemia (p value cannot be calculated),the

significance of which is difficult to assess, given the small number of patients studied.

3 patients (13.04%) in non MS group had hyperhomocysteinemia (p value cannot be calculated), the significance of which is difficult to assess, given the small number of patients studied

ANGIOGRAPHY:

TABLE 14: ANGIOGRPHY RESULTS IN MS/NON MS

ANGIOGRAM RESULT	MS		NON MS		p VALUE
	NO	%	NO	%	
SVD	39	58.2	16	69.56	0.335, NS
DVD	14	20.89	6	26.08	0.605, NS
TVD	14	20.89	1	4.34	0.066, NS

SVD = one vessel involved, DVD = two vessels involved

TVD= three vessels involved, NS = NIL SIGNIFICANT

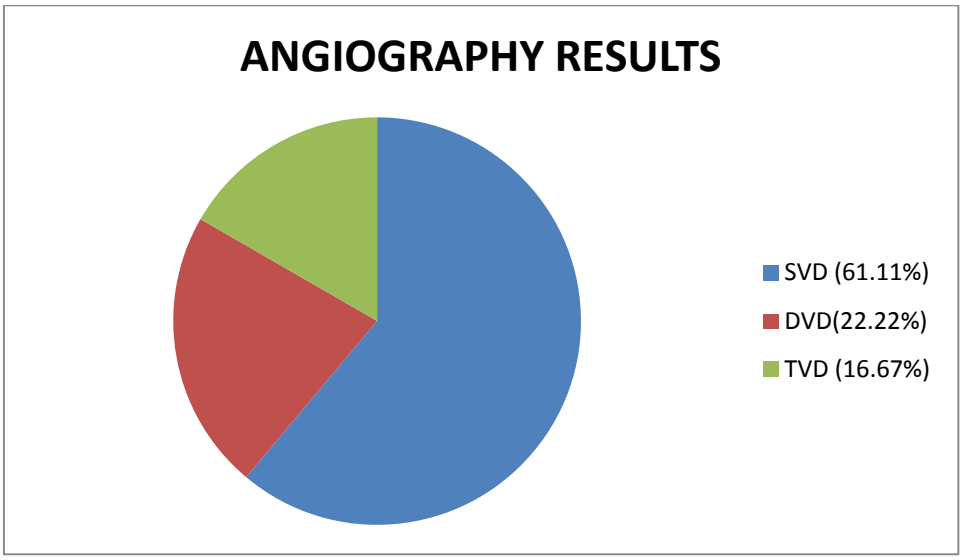
39 patients (58.20%) in MS group and 16 patients (69.56%) in non MS group had single vessel disease.

14 patients (20.89%) in MS and 6 patients (26.08%) in non MS group had double vessel disease.

14 patients (20.89%) in MS and 1 patient(4.34%) in non MS group had triple vessel disease.

p-value obtained were 0.335, 0.605 and 0.066 respectively which were statistically not significant.

FIGURE 9:



DISCUSSION

Syndrome X is a clustering of various factors responsible for development of DM and CVD. It comprises of abdominal adiposity/SHT/decreased HDL/ hypertriglyceridemia and intolerance to glucose. MS presence itself carries double the chance of developing atherosclerotic mediated CVD and 6 times the chance of developing DM.

Younger subjects with premature CAD, most of the time may have low cardiovascular disease risk estimates.MS is more commonly seen in this group of subjects necessitating multi-factorial risk approach for CAD prevention in these candidates with minimal risk for cardiovascular disease.

Its relation with acute coronary syndrome, MS was independent from various other confounding factors. Hence identification of subjects with MS will definitely be helpful in reducing long term risk, mortality and morbidity.

Several different criteria have been proposed for diagnosis of MS by various professional bodies. The most widely used one appears to be the one proposed by the IDF (International Diabetic Federation) which includes ethnic specific cut-offs for WC. There has been lot of controversy regarding whether to accept this concept of MS based on the

contention that it does not represent any abnormal patho-physiology and the risk attributed by MS is no different to that contributed by each of its individual factors.

However, the concept of MS is very important because it provides easy meaningful information which helps the general population and professionals, particularly to look for the presence of other causative factors in the same subject.

In the present study which included 90 cases of CAD, MS was present in 67 cases (74.44%).

TABLE 15: COMPARISON OF PREVALENCE OF MS WITH PREVIOUS STUDIES

Study	% of MS in CAD
Milani R[6] et al (2003)	58
Niomiya[245] et al (2004)	41.5
Levantesi G[246] et al (2005)	29
Schwartz G[247] et al (2005)	38
Zeller M[248] et al (2005)	46
Present Study	74.44

There is increasing evidence regarding development of atherosclerotic disease in patient with MS and hence its identification will definitely helpful to prevent further progression to over disease like CVD and overt diabetes. Irrespective of FRS estimate its identification in patient has related to increased cardio vascular disease risk[249].

In a cross sectional study large number of children and adolescent and around 30 percent of the adult population were found to have this MS[16,22,44].

Till to date little information is available about the presence and distribution of MS in young coronary artery disease patients[25,26]. Earlier studies have inferred that the presence of MS in young CAD patients is almost seen in half.

In studies conducted by Zarich et al[250], reported prevalence of MS in two third of the subjects studied regardless of their diabetic status and have focussed on the fact that all existing guidelines have not sufficiently estimated the risk of coronary artery disease in young population having MS.

Turhan et al[26] reported 37% prevalence of MS in Turkish patients with premature CAD. In keeping with earlier report MS was present in 74.4% of patients with premature CAD in our study [251]. Framingham risk

score was found to be less predictive in diagnosing MS in patients with diabetes mellitus[252].Diabetes epidemiology. collaborative analysis of diagnostic criteria in Europe have concluded the fact that among their study population person with lower CVD risk scoring and co existing MS had a significant high risk for fatal CVD than those without the syndrome [27].

In our study we evaluated the prevalence of MS in premature CAD patients taking into consideration the fact from previous studies that even after adjustment for other risk factors for CAD the presence of MS alone had been a major risk factor for CAD with 200% risk especially in a population with low Framingham Risk Score [249]. Hence we suggest that careful clinical assessment of MS to be a important tool in the hands of preventive medical care personnel and physicians as its prevalence can itself be considered to be a detrimental factor in assessing final end points in patients with CAD. In our study prevalence of MS is 74.4% in premature CAD while traditional risk factors for CAD like diabetes mellitus and systemic hypertension were 55.2% and 46.26% respectively. This again supports the inferences from previous studies that MS assessment alone can be a significant tool in estimation of risk for CAD incidence in young population.

The dynamic changing trends of lifestyles in the urban population and even the rural population to an extent can be indirectly highlighted from the fact that in our study we have 55.2% of population with diabetes unlike previous studies where the incidence of diabetes and obesity was seen in less than 30% of the study population [253,254]. This suggests that atherogenic diet intake associated with changing life style, sedentary mode of work and increased trends of physical inactivity have increased the incidence of MS . Further studies focussed on these lines are mandatory to identify the root cause for such drastic elevation in incidence of MS and other individual risk factors for CAD in our population which can help us in focussing on treatment and prevention of these risk factors. However even the well known traditional risk factors like (smoking and family history of CAD) for atherosclerosis have to be taken into account as many recent studies have shown greater incidence of these risk factors in young CAD patients.[21,253,254]. In our study however we had no statistical significance between smoking habit and prevalence of MS in patients with young CAD with a p value of 0.825.

In a study conducted by Uhl et al,159 patients aged less than forty years were studied and it was found that SHT and obesity were predominant component and was present in greater than 58% of the population studied[21]. In our study 46.26% of patients in MS group and

13.03% in non-MS group had hypertension which is comparatively similar to the previous studies mentioned. Another study done by Kelly et al on patients with less than 40 years of age who underwent CABG, family history of premature CAD and smoking were again the most prevalent factor[255]. In our study traditional risk factors like smoking, history of CAD in the family were all found to be insignificant with the p value of 0.825 and 0.448 respectively which is statistically insignificant

The prevalence of DM is 55.22% and that of systemic hypertension was 46.26% in patients with AMI in MS group in comparison with non MS group which showed DM- 21.73% ; SHT – 13.04%. Elevated fasting blood sugars were seen in 43 patients out of 67 (64.17%) of MS group while it was 9 patients out of 23 (39.13%) of non MS group.

Among 67 subjects with MS, 29 had only 3 out of 5 criteria for MS. Among this 29, 12 were diabetic and 17 were non-diabetic.24 patients met 4 out of 5 criteria with 12 diabetic and 12 non-diabetic patients. 14 out of 67 patients met all the 5 criteria for MS, comprising 13 diabetic and 1 non-diabetic patients.

Among MS group of the remaining 30 without diabetes only one person had all the MS criteria (whereas among the remaining 13 patients who met all the 5 criteria for MS all had overt diabetes), 12 patients met 4

out of 5 criteria and 17 patients met only 3 criteria for MS. This emphasis the fact that patients with DM are more prone for developing cardiovascular disease mortality than those without diabetes.

High fasting blood glucose or treatment for diabetes is one of the diagnostic criteria for MS as per IDF definition. Unlike other studies underestimation of MS on a patient whose is already on treatment for diabetes with is not possible in our study.

Of the 44 patients with high blood pressure, 31 already had systemic hypertension and MS was more prevalent in this group with p value of less than 0.01 which is statistically significant. The presence of diabetes mellitus and systemic hypertension were also associated with diastolic and systolic heart dysfunction affecting proper functioning of viable myocardium[256] explaining the higher incidence of heart failure in these patients. In our study, distribution of DM and SHT were high compared to previous other studies mentioned earlier which highlight the increased chance of developing complications in these patients in future and the need for aggressive control of the disease.

The average of HDL cholesterol was significantly lower and average value of triglycerides were significantly higher in MS group with p value of <0.05 and <0.01 respectively. Previously low HDL cholesterol was the most observed component[26] in both MS and non MS group with

mean values lower in the MS group. In our study, high triglycerides were the more prevalent component.

In a study carried out by Misra et al on MS in south Asians they found that triglyceride levels were high and the level of HDL was low ,in our study Serum triglycerides were very high i.e. 179.14 (97.5%) may be related to South Indians who have high percentage of body fat and lower muscle mass[257]. Additionally insulin resistance also reduces the concentration of lipoprotein lipase in the peripheral tissues[258].

The high triglycerides with low HDL cholesterol in our study may be due to triglycerides decreasing the production and increasing the clearance of HDL cholesterol from the circulation[258,259].

In our study, possibility of underestimation of lipid levels is unlikely as patients with dyslipidemia and lipid lowering drug therapy for the same were also included in the diagnostic criteria for MS.

South Asians when compared to other western nations have BMI comparatively low with relatively higher waist circumference. This can lead to under estimation of population at risk of developing MS when routine conventional criteria designed and framed for people in western countries were used. Considering this the IDF criteria were chosen for studying the actual prevalence of metabolic syndrome in the young

population affected by CAD, as IDF has ethnic and race specific WC cut-offs which could obviously avoid under estimation of population at risk of developing CAD by identifying appropriate distribution of MS in these community. The prevalence of MS is recently showing an increasing trend due to increased prevalence of traditional risk factors like DM, SHT, abdominal adiposity in the community all of which all comes under the shades of MS criteria. Hence IDF definition for MS with gender and race specific waist circumference cut off was used in this study. Of all the 5 criteria for MS, waist circumference was the one most prevalent in premature CAD patients with metabolic syndrome which is highly significant.

Thus looking for presence of MS alone helps predicting future development of CVD and diabetes. Thus we recommend the use of IDF criteria than conventional criteria to know the probable burden of cardiovascular risk in the community through the means of MS which can predict future development of CAD and DM and thereby helps professional organisations and the public to implement primary prevention strategies as early as possible in the form of exercise, anti-atherogenic diet, life style and behavioural modifications[260].

Though the type of coronary vessel involved viz., single vessel disease/ double vessel disease/ triple vessel disease is not significant here

with the p value of 0.335, 0.605, 0.066 respectively, the prevalence of Triple vessel disease is more common in MS than non MS group.

It is clear from the study that MS strongly predicts coronary artery disease and cardiovascular disease mortality than its individual components[261].

RECOMMENDATIONS

- In the Indian set up use of IDF consensus definition is the ideal one to diagnose MS and for risk stratification.
- In order to reduce the risk of cardiovascular disease morbidity and mortality, the need to assess for other components of MS when any one is detected should be emphasised to all health care professionals.
- Regular physical activity and healthy diet should be emphasised among young individuals for primary prevention of CAD.
- Awareness about the principal criterion (waist circumference) should be promoted and individuals to be encouraged to keep tabs on it.

LIMITATIONS

1. Those patients who met 4 out of 5 criteria for MS without the principal criteria (waist circumference more than 80 in women and more than 90 in men) were excluded from the MS group.

2. Number of female patients involved in the study was low

3. Due to time constraints the sample size had to be restricted.

CONCLUSION

- In our study, 90 cases of acute MI aged ≤ 45 were studied for metabolic syndrome using IDF criteria. MS was diagnosed in 67 of 90 cases studied.

- Waist circumference was followed by Diabetes mellitus /Systemic hypertension/ elevated BP / hypertriglyceridemia/ elevated FBS and decrease in fasting HDL arranged in the order of prevalence in the study group which was statistically significant.

- Among the 67 patients, 14 met all criteria for MS, 24subjects had 4 and 29 subjects had 3 of 5 MS criteria, With WC ≥ 80 for females and ≥ 90 for males being a definite criterion.

- The prevalence of alcohol, whether a smoker ,history of CAD in the family, dyslipidemia , and vessel involvement – SVD/DVD/TVD were same for both MS and non MS group.

- Thus it is obvious that MS predominates over other conventional criteria or scores in estimating the risk of developing MI and related complications and its prevalence in our study population is 74.4% which is very significant.

- Though people living in low income countries like India have lower risk factor for CVD, compared with high income countries, the rate of death due to CVD is highest in low income countries. This is because there is better control of risk factor due to frequent use of proven drugs to reduce the risk of deaths.

- Thus determinants like easy and timely access to health care and medicine, diagnosis of risk factor and treatment / control and greater awareness play an important role in preventing death. Hence the two means to counter the risk factors and decrease the mortality are health promotion and health care.

- Health promotion component is to raise awareness and risk reduction. This is better done by identifying at risk individuals by the presence of MS component in this group and providing health care facilities for early detection and effective treatment in order to prevent cardiovascular disease morbidity and mortality.

- From the study it is clear that IDF consensus definition for MS suits Indians best for identifying high risk individuals. Hence we recommend its use to help prevent CVD morbidity and mortality in younger individuals in whom it is difficult to estimate CVD risk.

- As the risk factors have an increasing trend in India so does the mortality. The cardiovascular crisis is waiting to worsen unless we improve the health care system.

- Hence risk factor modification, regular physical activity and healthy diet among young patients should be emphasised for primary prevention of CAD.

- The concept of metabolic syndrome is very important as it provides simple and comprehensive information to the public.The medical professional should assess for presence of all the MS parameters whenever necessary.

REFERENCES

1. Feinlib M, Harlik RJ, and Thom TJ. The changing pattern of ischaemic heart disease. J Cardiovascualr Med 1982;7:139.

2. Allison RB, Rodriguez FL, and Higgins EAClinicopathological correlation in coronary atherosclerosis. Four hundred thirty patient studies with postmortem coronary angiography. Circulation 1963;27:170.

3. Grundy JM, Cleemanji, Daniels SR, et al. American Heart Association. National Heart Lung, and Blood Institute. Diagnosis and management of metabolic syndrome : An American heart association / National Heart Lung and Blood Institute scientific statement. Circulation 2005;112(17):2735-52.

4. Third report of the National Cholesterol Education Program (NCEP) Expert panel on Detection, Evaluation, and Treatment of high blood cholesterol in adults (Adult Treatment Panel III) Final report. Circulation 2002; 106: 3146-3421.

5. Yajnik CS. The insulin resistance epidemic in India: fetal origins, later lifestyle or both? Nutr Rev 2001; 59: 1-9.

6. Milani RV, Lavie CJ. Prevalence and profile of metabolic syndrome in patients following acute coronary events and effects of therapeutic life style change with cardiac rehabilitation. Am J Cardiol 2003; 92(1): 50-54.

7. Haffner SM. The metabolic syndrome: Inflammation, Diabetes mellitus, and Cardiovascular disease. Am J Cardiol 2006; 97(suppl): 3A-11A

8. Munjal YP, Sarena A. Metabolic syndrome: Assessing Cardiometabolic risk, Chapter 50: In YP Munjal, Post-graduate medicine (Recent Advances in Medicine): JP Publishers: 2007; XXI: 461.

9. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2005, - prevalence, numerical estimates, and projections. Diabetes Care 1998; 21: 1414-31.

10. Kylin E. Studien uber das hypertonic – hyperglykamie – hyperurikamie syndrome. Zentralblatt fur Innere Medizin 1923; 44: 105-27.

11. Vague J. La differenciation sexuelle, facteur determinant des formes del'obesite. Press Med 1947; 30: 339-40.

12. Raven G. Role of insulin resistance in human disease. Diabetes 1988; 37: 1595-1607

13. Deedwania PC, Gupta R. Management issues in the metabolic syndrome. J Assoc Physicians India 2006; 54: 797-810.

14. Lemieux I, Pascot A, Couillard C, et al. Hypertriglyceridemic waist: a marker of atherogenic metabolic triad in men? Circulation 2000; 102: 179-84.

15. Alexander C.M., Landsman P.B., Teutsch., Haffner S.M.: NCEP-defined metabolic syndrome , diabetes and prevalence of coronary artery disease among NHANES III participants aged 50 yrs and older. Diabetes 52.1210-1214.2003; Abstract

16. Lakka H.M., Lakksonen D.E., Lakka T.A., et al. The metabolic syndrome and total and cardiovascular disease mortality in middle aged men. JAMA 288.2709-2716.2002; Abstarct

17. Sattar N., Gaw A., Scherbakova O., et al: metabolic syndrome with and without c-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Pervention Study. Circulation 108.414-419.2003; Abstract.

18. Perski A., Olsson G., Landou C., et al: Minimum heart rate and coronary atherosclerosis : independent relations to global severity and rate of progression of angiographic lesions in men with myocardial infarction at a young age . Am heart J 123.609-616.1992; Abstract

19. Towbin J.A., Bricker J.T., Garson , Jr. JrA.: Electrocardiographic criteria for diagnosis of acute myocardial infarction in childhood . Am J Cardiol 69.1545-1548.1992; Abstract

20. Weinberg I ., Rotenberg Z., Fuchs J., et al: Myocardial infarction in young adults under 30 yrs: risk factors and clinical course. Clin Cardiol 10.9-15.1987; Abstarct

21. Uhl G.S., Farrell P.W.: Myocardial infarction in young adults: risk factors and natural history. Am Heart J 105. 548-553.1983; Citation.

22. Ridker P.M., Burning J.E., Cook N.R., Rifai N.: C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-years follow-up of 14 719 initally healthy American women. Circulation 107.391-397.2003; Abstract

23. Baltali M., Gokcel A., Kiziltan H.T., et al: Association between the metabolic syndrome and newly diagnosed coronary artery disease . Diabetes Nutur Metab 16.169-175.2003; Abstarct

24. Solymoss B.C., Bourassa M., Lesperance J., et al: Incidence and clinical characteristics of the metabolic syndrome in patients with coronary artery disease. Coronary Artery Dis 14.207-212.2003; Abstract

25. Iribarren C., Go A.S., Husson G., et al: Metabolic syndrome and early-onset coronary artery disease: is the whole greater than its parts. J Am Coll Cardiol 48.1800.2006; Abstract

26. Turhan H., Yasar A.S., Basar N., et al: high prevalence of metabolic syndrome among young qomen with premature coronary artery disease. Coron Artery Dis 16. 37-40.2005; Abstract

27. The Diabetes Epidemiology: Collaborative analysis Of Diagnostic Criteria in Europe(DECODE) Study Group: Does diagnosis of the metabolic syndrome detect further men at high risk of cardiovascular death beyond those identified by a conventional cardiovascular risk score? The DECODE Study. Eur J Cardiovasc Prev Rehabil 14.192-199.2007;

28. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes 1988; 37:1595

29. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care 1991; 14:173.

30. Lindsay RS, Howard BV. Cardiovascular risk associated with the metabolic syndrome. Curr Diab Rep 2004; 4:64

31. Koh KK, Han SH, Quon MJ. Inflammatory markers and the metabolic syndrome: insights from therapeutic interventions. J Am Coll Cardiol 2005; 46:1978.

32. Grundy SM, Brewer HB Jr, Cleeman JI, et al. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004; 109:433..

33. Eckel RH, Kahn R, Robertson RM, Rizza RA. Preventing cardiovascular disease and diabetes: a call to action from the American Diabetes Association and the American Heart Association. Circulation 2006; 113:2943.

34. Grundy SM. Metabolic syndrome: a multiplex cardiovascular risk factor. J Clin Endocrinol Metab 2007; 92:399.

35. World health organisation (1999) definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. WHO, Geneva1999.

36. Grundy SM, Brewer HB Jr, Cleeman JI, Lenfant C. Definition of metabolic syndrome: Report of the national Heart Lung and Blood Institute / American Heart A ssociation conference on scientific issues related to definition. Circulation 2004; 109;433-438.

37. Balkau B , Charles MA . Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). Diabet Med 1999; 16:442-443.

38. Alberti KG,Zimmet P,Shaw J. The metabolic syndrome –a new worldwide definition. Lancet 2005; 366:1059-1062.

39. Alberti KG,Eckel RH,Grundy SM et al. Hormonizing the metabolic syndrome.A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention ; National Heart, lung and blood institute ;American heart association;world heart federation ; international atherosclerosis society ; and international association for the study of obesity . circulation 2009; 120: 1640-1645

40. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001; 285:2486.

41. Genuth S, Alberti KG, Bennett P, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003; 26:3160.

42. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005; 112:2735.

43. International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome, 2006. ttp://www.idf.org/webdata/docs/MetS_ def_update2006.pdf (Accessed on September 30, 2011).

44. Ford ES. Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the U.S. Diabetes Care 2005; 28:2745.

45. Adams RJ, Appleton S, Wilson DH, et al. Population comparison of two clinical approaches to the metabolic syndrome: implications of the new International Diabetes Federation consensus definition. Diabetes Care 2005; 28:2777.

46. Sandeep S,Gokulakrishnan K,Deepa M, Mohan V. Insulin resistance is associated with increased cardiovascular risk in Asian Indians with normal glucose tolerance—the Chennai Urban Rural Epidemiology Study (CURES-66).J Assoc Physicians India.2011;59:480-4.

47. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. Circulation 2003; 107:391.

48. .Festa A, D'Agostino R Jr, Howard G, et al. Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). Circulation 2000; 102:42.

49. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation 2003; 107:363.

50. Festa A, D'Agostino R Jr, Tracy RP, et al. Elevated levels of acute-phase proteins and plasminogen activator inhibitor-1 predict the development of type 2 diabetes: the insulin resistance atherosclerosis study. Diabetes 2002; 51:1131.

51. Pradhan AD, Manson JE, Rifai N, et al. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 2001; 286:327.

52. Hu FB, Meigs JB, Li TY, et al. Inflammatory markers and risk of developing type 2 diabetes in women. Diabetes 2004; 53:693.

53. Rutter MK, Meigs JB, Sullivan LM, et al. C-reactive protein, the metabolic yndrome, and prediction of cardiovascular events in the Framingham Offspring Study. Circulation 2004; 110:380.

54. Timpson NJ, Lawlor DA, Harbord RM, et al. C-reactive protein and its role in metabolic syndrome: mendelian randomisation study. Lancet 2005; 366:1954.

55. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest 2003; 111:1805.

56. Weyerc,Foley JE Bogardus C,et al .Enlarged subcutaneous abdominal adipocyte size, but not obesity itself ,predicts type II diabetes independent of insulin resistance .Diabetologia 2000;43:1498-506.

57. Joshi R Metabolic Syndrome – Emerging clusters of the Indian Phenotype. J Assoc Physicians India . 2003;51:445-6

58. Pi-sunyer .Metabolic syndrome in obesity.Obesity Research 2004 vol. 12.

59. Park YW, Zhu S, Palaniappan L, et al. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. Arch Intern Med 2003; 163:427.

60. Wilson PW, Kannel WB, Silbershatz H, D'Agostino RB. Clustering of metabolic factors and coronary heart disease. Arch Intern Med 1999; 159:1104.

61. Palaniappan L, Carnethon MR, Wang Y, et al. Predictors of the incident metabolic syndrome in adults: the Insulin Resistance Atherosclerosis Study. Diabetes Care 2004; 27:788.

62. Manson JE, Skerrett PJ, Greenland P, VanItallie TB. The escalating pandemics of obesity and sedentary lifestyle. A call to action for clinicians. Arch Intern Med 2004; 164:249.

63 .Ferreira I, Twisk JW, van Mechelen W, et al. Development of fatness, fitness, and lifestyle from adolescence to the age of 36 years: determinants of the metabolic syndrome in young adults: the amsterdam growth and health longitudinal study. Arch Intern Med 2005; 165:42.

64. Dhingra R, Sullivan L, Jacques PF, et al. Soft drink consumption and risk of developing cardiometabolic risk factors and the metabolic syndrome in middle-aged adults in the community. Circulation 2007; 116:480.

65 Lamberti JS, Olson D, Crilly JF, et al. Prevalence of the metabolic syndrome among patients receiving clozapine. Am J Psychiatry 2006; 163:1273.

66. LaMonte MJ, Barlow CE, Jurca R, et al. Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome: a prospective study of men and women. Circulation 2005; 112:505.

67. Panhuysen CI, Cupples LA, Wilson PW, et al. A genome scan for loci linked to quantitative insulin traits in persons without diabetes: the Framingham Offspring Study. Diabetologia 2003; 46:579.

68. Kannel WB, Abbott RD. Incidence and prognosis of unrecognized myocardial infarction. An update on the Framingham study. N Engl J Med 1984; 311:1144.

69. Fournier JA, Sánchez A, Quero J, et al. Myocardial infarction in men aged 40 years or less: a prospective clinical-angiographic study. Clin Cardiol 1996; 19:631.

70. Doughty M, Mehta R, Bruckman D, et al. Acute myocardial infarction in the young--The University of Michigan experience. Am Heart J 2002; 143:56.

71. Greenland P, Reicher-Reiss H, Goldbourt U, Behar S. In-hospital and 1-year mortality in 1,524 women after myocardial infarction. Comparison with 4,315 men. Circulation 1991; 83:484.

72. Cole JH, Miller JI 3rd, Sperling LS, Weintraub WS. Long-term follow-up of coronary artery disease presenting in young adults. J Am Coll Cardiol 2003; 41:521.

73 .Hoit BD, Gilpin EA, Henning H, et al. Myocardial infarction in young patients: an analysis by age subsets. Circulation 1986; 74:712.

74. Zimmerman FH, Cameron A, Fisher LD, Ng G. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (Coronary Artery Surgery Study Registry). J Am Coll Cardiol 1995; 26:654.

75. Wolfe MW, Vacek JL. Myocardial infarction in the young. Angiographic features and risk factor analysis of patients with myocardial infarction at or before the age of 35 years. Chest 1988; 94:926.

76. Barbash GI, White HD, Modan M, et al. Acute myocardial infarction in the young--the role of smoking. The Investigators of the International Tissue Plasminogen Activator/Streptokinase Mortality Trial. Eur Heart J 1995; 16:313.

77. Chen L, Chester M, Kaski JC. Clinical factors and angiographic features associated with premature coronary artery disease. Chest 1995; 108:364.

78. Rosenberg L, Kaufman DW, Helmrich SP, et al. Myocardial infarction and cigarette smoking in women younger than 50 years of age. JAMA 1985; 253:2965.

79. Bao W, Srinivasan SR, Wattigney WA, Berenson GS. The relation of parental cardiovascular disease to risk factors in children and young adults. The Bogalusa Heart Study. Circulation 1995; 91:365.

80. Gaeta G, De Michele M, Cuomo S, et al. Arterial abnormalities in the offspring of patients with premature myocardial infarction. N Engl J Med 2000; 343:840.

81. Malmberg K, Båvenholm P, Hamsten A. Clinical and biochemical factors associated with prognosis after myocardial infarction at a young age. J Am Coll Cardiol 1994; 24:592.

82. McGill HC Jr, McMahan CA, Herderick EE, et al. Obesity accelerates the progression of coronary atherosclerosis in young men. Circulation 2002; 105:2712.

83. Wilson PW, D'Agostino RB, Sullivan L, et al. Overweight and obesity as determinants of cardiovascular risk: the Framingham experience. Arch Intern Med 2002; 162:1867.

84. Sastry S, Riding G, Morris J, et al. Young Adult Myocardial Infarction and Ischemic Stroke: the role of paradoxical embolism and thrombophilia (The YAMIS Study). J Am Coll Cardiol 2006; 48:686.

85 Agostoni P, Gasparini G, Destro G. Acute myocardial infarction probably caused by paradoxical embolus in a pregnant woman. Heart 2004; 90:e12

86. Rosenberg L, Palmer JR, Rao RS, Shapiro S. Low-dose oral contraceptive use and the risk of myocardial infarction. Arch Intern Med 2001; 161:1065

87. Qureshi AI, Suri MF, Guterman LR, Hopkins LN. Cocaine use and the likelihood of nonfatal myocardial infarction and stroke: data from the Third National Health and Nutrition Examination Survey. Circulation 2001; 103:502.

88. Mansourati J, Da Costa A, Munier S, et al. Prevalence of factor V Leiden in patients with myocardial infarction and normal coronary angiography. Thromb Haemost 2000; 83:822.

89. Chang PP, Ford DE, Meoni LA, et al. Anger in young men and subsequent premature cardiovascular disease: the precursors study. Arch Intern Med 2002; 162:901.

90. Klein LW, Agarwal JB, Herlich MB, et al. Prognosis of symptomatic coronary artery disease in young adults aged 40 years or less. Am J Cardiol 1987; 60:1269.

91. Chen L, Chester M, Kaski JC. Clinical factors and angiographic features associated with premature coronary artery disease. Chest 1995; 108:364.

92. Sarda L, Colin P, Boccara F, et al. Myocarditis in patients with clinical presentation of myocardial infarction and normal coronary angiograms. J Am Coll Cardiol 2001; 37:786.

93. Karjalainen J, Heikkilä J. Incidence of three presentations of acute myocarditis in young men in military service. A 20-year experience. Eur Heart J 1999; 20:1120.

94. Davia JE, Hallal FJ, Cheitlin MD, et al. Coronary artery disease in young patients: arteriographic and clinical review of 40 cases aged 35 and under. Am Heart J 1974; 87:689.

95. Holmes DR Jr, White HD, Pieper KS, et al. Effect of age on outcome with primary angioplasty versus thrombolysis. J Am Coll Cardiol 1999; 33:412.

96. Füllhaas JU, Rickenbacher P, Pfisterer M, Ritz R. Long-term prognosis of young patients after myocardial infarction in the thrombolytic era. Clin Cardiol 1997; 20:993.

97. Mehan VK, Urban P, Dorsaz PA, Meier B. Coronary angioplasty in the young: procedural results and late outcome. J Invasive Cardiol 1994; 6:202.

98. FitzGibbon GM, Hamilton MG, Leach AJ, et al. Coronary artery disease and coronary bypass grafting in young men: experience with 138 subjects 39 years of age and younger. J Am Coll Cardiol 1987; 9:977.

99. Ng WK, Vedder M, Whitlock RM, et al. Coronary revascularisation in young adults. Eur J Cardiothorac Surg 1997; 11:732.

100. Janusz h.skalski.myocardial infarction and angina pectorisin the history of polish medicine.part 1.discovery and understanding of the disease. Pol arch med wewn 2008;118(4):xx-xx.

101. Hberden W.Some account of a disorder of the breast. Medical transactions 1772;2:59-67

102. Hektoen l. Embolism of the left coronary artery ;sudden death. Med Newsl (Lond)1892;61:210

103. Obrastzov WP ,Straschesko ND .Zur Kenntnis Der Thrombose Der Koronararterien Des Herzens .Z Klin Med 1910;71:116-32

104. Herrick JB .Certain clinical features of sudden obstruction of coronary arteries .Jama 1912;59:2015-20

105. IDEM .Thrombosis of the coronary arteries.Jama 1919;72:387-90

106. Kannel WB ,Dawber TR, Kagan A ,Revotskie N, Stokes J III .Factors of risk in the development of coronary heart disease- six year followup experience: the Framingham study .Am J Intern Med 1961;55:33-50.

107. NHLBL fact book ,fiscal year 2010.Bethesda,MD:National Heart Lung and Blood Institute , February 2010 (http://www.nhlbi,nih.gov/about/factpdf.htm)

108 . Julian DJ.Treatment of cardiac arrest in acute myocardial ischemia and infarction.Lancet 1961;2:840-4.

109. The works of Willial Hervey,M.D (an anatomical disquisition on the motion of heart and blood i animals),London ,1628.willis R ,Trans .London:New Sydenham Society,1847.

110 . Mueller RL, Sanborn TA. The history of interventional cardiology :cardiac catheterization, angioplasty, and related interventions .Am Heart J 1995;129:146-72.

111. forssman w. catheterization of the right heart .klinwochenschr 1929; 8:2085-7.

112. Cournand AF,Ranges HS .Catheterization of the right auricle in man. Proc Soc Exp Bio Med 1941;46:462-6.

113. Sones FM Jr.Shirey EK. Cine coronary arteriography. Mod concepts Cardiovasc Dis 962;31:735.

114. Gibbon JH Jr . Application of mechanical heart and lung apparatus to cardiac surgery.Minn Med 1954;37:171-5

115. Surruys P,Degertekin M ,Tanabe K,et al. Intravascular ultrasound findings in the multicenter, double blined, randomised RAVEL (Randomised study with the sirolismus eluting balloon-expandable stent in the treatment of patient with denovo native coronary artery Lesions) trial. Circulation 2002; 106:798-803.

116. Maroko PR ,Kjekshus JK ,Sobel BE,et al . factors influencing infarct size following experimental coronary artery occlusionin. Circulation 1971;43:67-82.

117. Chazov EI , Mateeva LS ,Mazaev AV,Sargin KE, Sardovskaia GV , Ruda MI. Intra coronary administration of fibrinolysin in acute myocardial infarct.Ter Arkh 1976;48:8-19.

118. Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GSSI). Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet 1986; 1:397-402.

119. ISIS-2 Colloborative Group. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2 . Lancet 1988; 2:349-60.

120. Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. N Engl Med 1993; 328:673-9.

121. A Tale of Coronary Artery Disease and Myocardial Infarction. Elizabeth G. Nabel, and Eugene Braunwald, N Engl J Med 2012:366;1 nejm.62 org.

122. Pfeffer MA, Braunwald E, Moye LA et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction : results of the Survival and Ventricular Enlargement trial. N Engl J Med 1992; 322: 699-77

123. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002; 346: 877-83

124. Burkhardt JD, Wilkoff BL. Interventional electrophysiology and cardic resynchronisation therapy: delivering electrical therapies for heart failure. Circulation 2007; 115:2208-20

125. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuos flow left ventricular assist device. N Engl J Med 2009; 361:2241-51.

126. Jessup M, Greenberg H, Mancini D et al. Calcium Up regulation by Percutaneous Administration of Gene Therapy in Cardiac Disease (CUPID): a phase 2 trial of intracoronary gene therapy of sarcoplasmic reticulum Ca2+- ATPase in patients with advanced heart failure. Circulation 2011; 124:304-13

127. Cannon CP, Braunwald E, McCabe CH, et al.Intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl Med 2004; 350:1495-504.[Erratum, N Engl J Med 2006; 354:778.

128. Mega JL, Braunwald e, Wiviott Sd, et al. Rivaroxaban in patients with a recent acute coronary syndrome. N Engl J Med 2012; 366:9-19.

129. Davies MJ , Woolf N, Robertson WB. Pathology of acute myocardial infarction with particular reference to occlusive coronary thrombi. Br Heart J 1976; 38:659-64.

130. Furchgott RF , Zawadzki JV. The obligatory role of endothelial cells in relaxation of arterial smooth muscle by acetylcholine. Nature 1980; 288:373-6. Ignarro LJ, Buga GM, Wood KS, et al.

131. Endothelium – derived relaxing factor prodecued and released from artery and vein is nitric oxide. Proc Natl Acad Sci U S A 1987; 84:9265-9.

132. Rapoport RM, Drazin MB, Murad F. Endothelium- dependent relaxation in rat aorta may be mediated through cyclic GMP-dependent protein phosphorylation. Nature 1983; 306:174-6. Ludmer PL, Selwyn AP, Shook TL, et al.

133. Paradoxical vasoconstriction induced by acetyl choline in atherosclerotic coronary arteries. N Engl J Med 1986; 315: 1046-51

134. Borissoff JI, Spornk HMH, ten Cate H. The haemostatic system as a modulator od atherosclerosis. N Engl J Med 2011; 364: 1746-50

135. Brown MS, Hobbs HH, Golstein JL. Familial hypercholesterolemia. In/; Valle D, BEaudet AL, Vogelstein B, Kinzler KW, Antonarakis SA, Ballabio A, eds. The online metabolic and molecular bases of inherited disease. Chapter 120 (http:// www.ommbid.com/ OMMBID/a/c.html/lipids/familial hypercholesterolemia).

136. Golstein JL, Brown MS. History of discovery: the LDL receptor. Arterioscler Thromb Vasc Biol 2009; 29-431-8.

137. Endo A. The discovery and development of HMG- Co-A inhibitors. J Lipid Res 1 992; 33: 1569-82

138. Brown MS, Goldstein JL. A receptor mediated pathway for cholesterol homeostasis. Science 1986; 232:34-47

139. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastin on coronary events after myocardial infarction in patients with average cholesterol levels: results of the Cholesterol and Recurrent Events (CARE) trial. N Engl J Med 1996; 335:1001-9.

140. Scandinavian Sinvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344:1383-9

141. Ridker PM, Cannon Cp, Morrow D et al. C-reactive protein levels and outcomes after statin therapy. N Engl J Med 2005; 352:20-8.

142. Ridker PM, Danielson E, Fonseca FA, et al. Reduction in C-reactive protein levels and LDL Cholesterol and cardiovascular event rates after initiation of rosuvastatin: a perspective study of the JUPITER trial. Lancet 2009; 373:1175-82

143. Cannon CP, Shah S, dansky HM , et al. Safety of anacetrapib in patients with or at high risk for coronary artery disease.N Engl J Med 2010; 363:2406-15

144. Nabel EG. Cardiovascular Disease. N Engl J Med 2003; 349:60-72.[Erratum, N Engl J Med 2003; 39:620.] ,

145. O'Donnell CJ, Nabel EG. Genomics of cardiovascular disease. N Engl j Med 2011; 365:2098-109.

146. Mega JL, Close SL, Wiviott SD, et al. Cytochrome P-450 polymorphosis and response to clopidogrel. N Engl J Med 2009; 360: 354-62

147. Musunuru K, Domain IJ, Chien KR. Stem cell models of cardiac development and disease. Annu Rev Dev Biol 2010; 26: 667-87.

148. Potente M, Gerhardt H, Carmeliet P. Basic and therapeutic aspects of angiogenesis. Cell 2011; 146:873-87.

149. Williams AR, Hare JM. Mesenchymal stem cells : biology, pathophysilogy, translational findings and therapeutic indications for cardiac disease. Circ Res 2011; 109:923-40

150. Hansson EM, Lindsay ME, Chien KR. Regeneration next: toward heart stem cell therapeutics. Cell Stem cell 2009; 5:364-77.

151. India – Human Development Fact Sheet . Accessed23 Jun 2005. URL: http://hdrc.undp.org.in/APRI/hds/hdfct/INdia.htm.

152. Sharma SP, Xenos P.1992. Ageing in India : Demographic background and analysis based on census materials. Occasional paper nr 2 of 1992. New Delhi : Office of the Registrar General and Census Commissioner.

153. Enas EA, Senthil Kumar a. 2001. Coronary Artery Disease in Asian Indians : an update and review [online]. Internet J Cardiol, I.Accessed 15 Feb 2005. URL: http;//www.ispub.com/ostia/index.php?xmlFile

154. Enas EA, Garg A, Davidnson Ma et al. 1996 . Coronary Artery Disease and its risk factors in the first generation immigrant Asian Indians to the United States of America. Indian Heart J, 48:343-54.,

155. Gupta R.1997.Epidemiological evolution and rise of coronary heart disease in India. South Asian J Prev Cardiol, 1:14-20.,

156. Enas A, Yusuf S. 1999. Third Meeting of the International Working group on Coronary Artery Disease in South Asians. Indian Heart J, 51:99-103. ,

157. Ghaffar A, Reddy KS, Singhi M.2004. Burden of non-communicable diseases in South Asia. BMJ, 328:807-10.

158. Reddy KS. 1993. Cardiovascular disease in India. World Health Stat Q, 46:101-7

159. Gupta SP, Malhotra KC.1975.Urban-rural trends in epidemiology of coronary heart disease. J Assoc Physicians India , 23:885-92. ,

160. Reddy KS. 1998. Rising burden of cardiovascular disease in India. In Sethi KK (ed). Coronary Artery Disease in Indians: a global perspective. Mumbai : Cardiological Society of India .p63-72

161. Begom R, Singh RB. 1995. Prevalence of coronary artery disease and its risk factors in the urban population of South and North India. Acta Cardiol,50:227-40.,

162. Ramachandran A, Snehalatha C, Latha E, et al. 1998. Clustering of cardiovascular risk factors in urban Asian Indians. Diabetes Care, 21:967-71.

163. Mohan V, deepa R, Rani SS, et al.2001. Prevalence of coronary artery disease and its relationship to lipid ina selected population in South India. J Am Coll Cardioal, 38:682-7

164. Reddy KS. 1998. Rising burden of cardiovascular disease in India. In Sethi KK (ed). Coronary Artery Disease in Indians: a global perspective. Mumbai : Cardiological Society of India .p63-72., Dewan BD, Malhotra K, Gupta S.1974. Epidemiological study of coronary heart disease in a rural community in Haryana. Indian Heart J, 26:68-78.

165. Harris RB, Weissfield LA. 1991. Gender differences in the reliability of reporting symptoms of angina pectoris. J Clin Epidemiol, 44:1071-8.

166. Gupta R, Gupta VP, Ahulwalia NS. 1994. Educational status, coronary heart disease and coronary risk factor prevalence ina rural population in India. BMJ, 307:1332-6.,

167. Wander GS, Khurana Sb, Gulati R, et al. 1994. Epidemiology of Coronary heart disease in a rural Punjab Population – prevalence and correlation with various risk factors. Indian Heart J. 46:319-23.

168. Singh RB, Ghosh S, Niaz Am et al. 1995.Epidemiological study diet and coronary risk factors in relation to central obesity and insulin levels in rural and urban populations of north India. INT j Cardiol, 47:245-55

169. Kutty RV , Balakrishnan K, Jayasree A, et al. 1993. Prevalence of coronary artery disease in the rural population of Thiruvananthapuram district, Kerala, India. Int J Cardiol, 39:59-70

170. Mammi MVI , Pavithran P,RAhman PA et al. Acute MI in North Kerala. A 20 year hospital based study. Indian Heart J. 1991;43:93-6.,

171. Negus BH, Williard JE, Glamann DB, et al. Coronary anatomy and prognosis of young asymptomatic survivors of myocardial infarction. Am J Med.1994; 96:35 Half of the CV4-8.

172. Murray CJL , Lopez AD 1994. Global Comparative assessments in the health sector. Geneva , Switzerland: World Health Organisation Denis Xavier , Prem Pais, P J Devereaux, 2008 Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data Lancet 2008; 371:1435-42

173. Yusuf S, Hawken S, OUnpuu S et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52countries (the INTERHEART study): case- control study. Lancet. 2004; 364:937-52.

174. Davidson ME, Enas EA, Thomas I. 1991. High Prevalence of low HDl-C levels and other dyslipidemic disorders in the Asian Indians in the United States. Proceedings of the National Conference on Cholesterol and High Blood Pressure Control, Washington..

175. Enas EA, Davidson ME, Nair V et al.1991. Prevalence of coronary heart disease CHD) and its risk factors in Asian migrants to the United States.9th International Symposium on Atherosclerosis. Rosemont, IL: InternationalAtherosclerosis Society. p267.,

176. Jha P, Enas EA, Yusuf S. 1993. Coronary artery disease in Asian Indians: prevalence and risk factors. Asian Am Pacific Islander J Health, 1:163-75., 177.Bhalodkar NC, Blum S, Rana T, et al.2004. Comparison of levels of large and small high density lipoprotein cholesterol in Asian Indian men compared with Caucasian men in the Framingham Offspring study. Am J cardiol, 94:1561-3.,

178. Hughes LO,RAval U, Raftery EB.1989. first myocardial infarctions in Asian and white men. BMJ, 298:1345-50

179. Enas EA, Garg A, Davidnson Ma et al. 1996 . Coronary Artery Disease and its risk factors in the first generation immigrant Asian Indians to the United States of America. Indian Heart J, 48:343-54.

180. Mosca L, Manson JE, Sutherland SE et al. 1997. Cardiovascular disease in women : a statement for healthcare professionals from the American Heart Association. Circulation, 96:2468-82.

181. Marrugat J, Gil M, Masia R et al. 1998. Mortality differences between men and women following first myocardial infarction. RESCATE Investigators. JAMA, 280:1405-9,

182. Vaccarino V , Krumholz HM , Yarzebski J , et al.2001. Sex Differencees in 2- year mortality after hospital discharge for myocardial infarction. Ann Intern Med, 134:173-81.,

183. Mak KH, Kark JD, Chia KS, et al. 2004. Ethnic variations in female vulnerability after an acute coronary event. Heart, 90:621-6.,

184. Jenkins JS, Flaker GC, Nolte B, et al. 1994. Causes of higher in-hospital mortality in women than men after acute myocardial infarction: the Framingham study. Am J Cardiol, 73:319-22.,

185. Assmann G, Cullen P, Schulte H.2002. Simple scoring scheme for calculating risk of acute coronary events based on the 10 year follow up of the Prospective Cardiovascular Munster (PROCAM) study. Circulation, 105:310-15

185. Gupta R. Gupta VP, saran M et al.2002. Prevalence of coronary heart disease and risk factors in an urban Indian population: Jaipur Heart Watch-2. Indian Heart j, 54:59-66.

186. Ramachandran A, Snehalatha C, Kapur A, et al.2001. High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia, 44:1094-101

187. Kaul U, Dogra B, Manchanda SC, et al.1986.Myocardial Infarction in young Indian patients: risk factors and coronary arteriographic profile. Am Heart j, 112:71-5.

188. Maity Ak, Das MK, Chatterjee SS, et al.1989. Prognostic significance of risk factors in acute myocardial infarction in young. Indian Heart j, 41:288-91.,

189. Dave TH, Waisr HS, prabhakaran D, et al.1991. Profile of coronary artery disease in Indian Women: correlation of clinical, non-invasive and coronary angiographic findings. Indian Heart J, 43:25-9.,

190. Usha S, Shah Cv, Sharma Sen.1991. Myocardial infarction in the young. J.Assoc Physicians India, 39:525-6.,

191. Pinto RJ, Bhagwat AR, Loya YS, et al.1992. Coronary artery disease in premenopausal Indian women : risk factors and angiographic profile. Indian Heart J, 44:99-101.,

192. Biswas PK, Dasbiswas A, Roy S et al. 1995.Risk Factors and angiographic profile of coronary artery disease in young. J Indian Med Assoc, 93:90-2,94.,

193. Goel PK. Bharti BB, Pandey Cm et al. 2003. A tertiary care hospital based study of conventional risk factors including lipid profile in proven coronary artery disease. Indian Heart J, 55:234-40.,

194 . Patil SS, joshi R, Gupta G et al.2004. Risk factors for acute myocardial infarction in rural population of central India: a hospital based case - control study. Natl Med J India, 17:189-94

195. Mohan V, deepa R, Rani SS, et al.2001. Prevalence of coronary artery disease and its relationship to lipid ina selected population in South India. J Am Coll Cardioal, 38:682-7

196. Patil SS, joshi R, Gupta G et al.2004. Risk factors for acute myocardial infarction in rural population of central India: a hospital based case - control study. Natl Med J India, 17:189-94

197. Chen L, Chester M, Kaski J.C 1995 Clinical factors and angiographic features associated with premature coronary artery disease Chest/108/2

198. American Diabetes Association : Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33 (Suppl 1):S62.

199. Wild S, Roglic G, Green A , et al: Global prevalence of diabetes: Estimates for the y ear 2000 and Projections for the year 2030. Diabetes Care 2004; 27:1047.

200. Preis SR, Hwang SJ, Coady S et al: Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham Heart Study, 1950 to 2005. Circulation 2009; 119:1728.

201. Holman RR, Paul SK, Bethel MA et al : 10-year follow up of intensive glucose control in type 2 diabetes. N Engl J Med 1577; 369:2008.,

201. Gerstein HC, Miller ME, Byington RP, et al: Effects of intensive glucose lowering in type 2 diabetes . N Engl J Med 2008; 358:2545.,

203. Patel A, MacMahon S, Chalmers J et al: Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med 2008;358:2560.

204. Fang J, Aldermann MH : Impact of the increasing burden of diabetes on acute myocardial infarction in New York City: 1990-2000. Diabetes ; 55:768

205. Wiviott SD, Braunwald E Angiolillo DJ, et al : Greater clinical benefit of more intensive oral anti-platelet therapy with prasugrel in patients with diabetes mellitus in the trial to assess improvement in therapeutic outcomes by optimising platelet inhibition with prasugrel – Thrombolysis in myocardial infarction. 38. Circulation 2008; 118:1626.

206. Kosiborod M, Inzucchi SE , Krumholz HM, et al: Glucose normalisation and outcome in patients with acute myocardial infarction. Arch Intern Med 2009; 169:438.

207. Ingelsson E , Sundstrom J, Arnlov J, et al: Insulin resistance and risk of congestive heart failure. JAMA 2005; 294:334

208. Hu FB ,Stampfer MJ , Haffner SM, et al: Elevated risk of cardiovascular disease prior to clinical diagnosis of diabetes. Diabetes Care 2002; 25:1129.

209. Earl S. Ford , Guixiang Zhao, Chaoyang Li : Pre –Diabetes and Risk for Cardio Vascular Disease, A Systemic Review of the Evidence. JACC 2010; Vol 55, 1310-17 Vol 1

210. The DECODE Study Group. Glucose tolerance and cardiovascular mortality: Comparison of fasting and 2-hour diagnostic criteria. Arch Intern Med 2001; 161:397-405

211. Rijkelijkhuizen JM, Nijpels G, Heine RJ, Boulter LM, Stehouwer CD, Dekker JM. High risk of cardiovascular mortality in individuals with impaired fasting glucose is explained by conversion to diabetes: the Hoorn study. Diabetes Care 2007; 30:332-6.

212. Ruderman N , Chisholm D , Pi-Sunyer X, et al : The metabolically obese , normal-weight individual revisted. Diabetes 1998; 47:699-713.

213. Banerji MA , Faridi N, Atluri R, et al : Body composition , Visceral fat, leptin and insulin resistance Asian Indian men. J Clin Endocrinol Metab 1999; 84:137-144.

214. Enas A. Enas, Vishwanathan Mohan, Mohan Deepa , Syed Farooq, Suraj Pazhoor, Hancy Chennikkara: The metabolic syndrome and dyslipidemia among Asian Indians : A Population with High Rates of Diabetes and Premature Coronary Artery Disease JCMS.2007; 2:267-275

215. Whincup PH, Gilg JA, Papacosta O, et al. Early evidence of ethnic differences in cardiovascular risk : cross sectional comparison of British South Asian and white children . BMJ 2002; 324:635.

216. Anand SS , Yusuf S, Vuksan V et al. Differences in risk factors , atherosclerosis and cardiovascular disease between ethnic groups in Canada. The Study of Health Assessment and Risk in ethnic Groups. (SHARE). Lancet, 2000; 356:279-284

217. Grundy SM, Cleeman JI, Daniels SR, et . Diagnosis and management of the metabolic syndrome : an American Heart Association/ National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005; 112:2735-2752.

218. O'hare JP, Raymond NT, MUGHal S , et al. Evaluation of delivery of enhanced diabetes care to patients of South Asian ethnicity: the United Kingdom Asian Diabetes Study (UKADS).Diabet. Med.2004; 21:1357-1365.

219. Mohan V, Deepa M, Farroq S, et al. Anthropppometric cut points for identification of cardio metabolic risk factors in an urban Asian Indian population. Metabolism 2007; 56: 961-968

220. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome – A new world wide definition. Lancet 2005; 366:1059- 1062.

221. Grundy SM, Cleeman JI, Daniels SR, et al, on behalf of the American Heart Association and the National, Heart , Lung and Blood Institute. Diagnosis and management of the metabolic syndrome: An American Heart Association/ National Heart Ling and Blood Institute Scientific statement : executive summary. Circulation 2005; 112:2735-2752

222. Grundy SM. Metabolic syndrome: connecting and reconciling cardiovascular and diabetes worlds. Jam Coll Cardiol. 2006;47 :1093-1100

223. Lind L,Hanni A, Lithell H, Hvarfner A, Sorensen OH, Ljunghall S.Vitamin D is related to blod pressure and other cardiovascular risk factor in middle aged men.Am J Hypertens 1995;8:894-901.

224. Pittas AG,Lau J ,Hu FB,Dawson –Hughes B.The role of vitamin D and calcium in type 2 diabetes. A systematic review and metaanalysis. J Clin Endocronol Metab 2007;92:2017-2029.

225. Bland R,Markovic D,Hills CE, Hughes SV,Chan SL,Squires PE,Hewison M. Expression of 25-hydroxy vitamin D3-1alpha hydroxylase in pancreatic islets. J Steroid Biochem Mol Biol 2004;89-90:121-125.

226. Subba Reddy Vanga, Mathew good,patricia a,howard,james L ,vecek. Role of vitaminD in cardiovascular health.Am J Cardiol 2010;106:798-805.#.

227. Zeitz U,Weber K,Soegiarta DW,Wolf e, Balling R,Erben RE. Impaired insulin secretary capacity in mice lacking a functional vitamin D receptor.FASEB J 2003;17:509-511.

228. Bourlan PM, Faure Dussert A,Billaudel B. The denovo synthesis of numerous proteins is decreased during vitamin D deficiency and is gradually restored by 1,25-dihydroxy vitamin D3 repletion in the islets of langerhans of rats. J Endocrinol 1999;162:101-109.

229. Mitri J,Dawson Hughes B,Hu FB,Pitas AG.Effects of vitamin D and calcium supplementation on pancreatic β-cell function,insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomised contolled trial. Am J Clin Nutr.2011;94:486-94.

230. Maestro B,Campion J,Davila N,Calle C.Stimulation by 1,25-dihydroxy vitamin D3 of insulin receptor expression and insulin responsiveness for glucose transportin u-937 human promonocytic cells.Endocr J 2000;47:383-391.

231. The EURODIAB substudy 2 study group. Vitamin D supplementation in early childhood and risk for type I (insulin dependent) diabetes mellitus.Diabetologia 1999;42:51-54.

232. Microalbuminuria : Is a valid predictor of cardiovascular risk; Rodrigo Tagle et al-A review Cliveland Clinic Journal of Medicine Vol 70;Number 3,March 2003.

233. Microalbuminuria & risk for cardiovascular disease.analysis of potential mechanisms.Coen D.A. et al.J.Am.Soc.Nephrol17:2106-2111,2006.

234. Microalbuminuria & cardiovascular disease-Mini Review ;Mathew.R. Weir.Clin J.Am Soc Nephrol 2:581-590,2007.

235. Lisa de las Fuentes,Angela L.Brown,Santhosh J.Mathews et al. Metabolic syndrome is associated with abnormal left ventricular diastolic function independent of left ventricular mass. Eur Heart J,2007 Mar;2(5):553-9.

236. Hisashi Masaguta ,Shiochi Senda , Fuminori Goda Left Ventricular Diastolic Dysfunction Assessed by echocardiography in Metabolic Syndrome .Hypertension Research 2006,29:897-903

237. AzevedoA et al "increasing number of components of metabolic syndrome and cardiac structural and functional abnormalities: cross-sectional study of the general population "BMC Cardio Vascular Disorders 2007.

238. Mukherjee D, Hsu A, Moliterno DJ,et al.Risk factors for premature coronary artery disease and determinants of adverse outcomes after revascularisation in patients 40 years old. Am J Cardiol 2003;92:1465-7.

239. Chua SK, Hung HF, Shyu KG,et al. Acute ST elevation myocardial infarction in young patients: 15 years of experience in a single center. Clin Cardiol 33;3:140-8.

240. Barbash gi, white HD,Modan M, et al. Acute myocardial infarction in the young: the role of smoking.the investigators of the international tissue plasminogen activator/streptokinase mortality trial. Eur Heart J 1995;16:313-6.

241. Hoit BD, Glipin EA, Henning H,et al. Myocardial infarction in young patients :an analysis by age subsets. Circulation 1986;74:712-21.

242. Kallirroi Kalantzi, Panagiotis Korantzopoulos,et al. American Heart Journal- Volume 155, Issue 3 (March 2008)

243. Reaven G. The metabolic syndrome or the insulin resistance syndrome? Different names, different concepts, and different goals. Endocrinal Metab Clin N-Am 2004;33:283-303.

244. Alpert JS,Thygesan K, Antman E, Bassand JP. Myocardial infarction redefined: a consensus document of the Joint European society of Cardiology/American college of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000;36:959-69.

245. Ninomiya JK, L'Italien G, criqui mh, whyte jl, gamst a, chen rs. Association of the metabolic syndrome with history of myocardial infarction and stroke in the third national health and nutrition examination survey. Circulation 2004;109:42-46.

246. Levantesi G, Macchia A, Marfici RM, Franzosi MG, Maggloni AP, Nicolosi GL,et al. Metabolic syndrome and risk of cardiovascular events after myocardial infarction. J Am Coll Cardiol 2005;46(2) 277-83.

247. Schwartz,Szarek M, Losson A, Sasiela W. Relation of characteristics of metabolic syndrome to short term prognosis and effects of intensive statin therapy after acute coronary syndrome. Diabetes care 2005;28:2508-13.

248. Zeller M, Gabriel P, Ravisy J, Laurent Y, Manifican LJ, Hullier et al. Prevalence and impact of metabolic syndrome on hospital outcomes in acute myocardial infarction.

249. Girman CJ, Rhodes T, Mercuri M,et al. The metabolic syndrome and risk of major coronary eventsin the Scandinavian simvastatin survival study (4S)and the Air Force /Texas coronary atherosclerosis prevention study. Am J Cardiol 93.136-141.2004.

250. Zarich S,Luciano C, Hulford J, Abdullah A. Prevalence of metabolic syndrome in young patients with acute MI : Does the Framingham risk score underestimate cardiovascular risk in this population. Diab Vasc Dis Res 3.103 -107:2006.

251 .Stern MP,Williams K, Gonzalez – Villalpandu C,et al. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and /or cardiovascular disease. Diabetes Care 27.2676-2681.2004.

252. Wannamethee S.G, Shaper A.G, Lennon L, Morris R.W.Metabolic Syndrome Vs Framingham risk score for prediction of coronary artery disease,stroke,and type 2 diabetes mellitus. Arch Intern Med 165.2644-2650.2005.

253. Hamsten A, Wiman B, Defaire U,Blomback M.Increased plasma levels of a rapid inhibitor of tissue plasminogen activator in young survivors of myocardial infarction. N Engl J Med 1985;313:1557-1563.

254. Wolfe MW, vacek jl, myocardial infarction in the young. Chest 1988;94:926-930.

255. Kelly ME,Deliria GA,Najafi H. Coronary artery bypass surgery in patients less than 40 years of age. Chest1988;94:1138-1141.

256. Aronson D, Ray field EJ, Chesebro JH. Mechanism determining course and outcome of diabetes patients who have had myocardial infarction. Ann Intern Med 1997;126:296-306.

257. Misra A,Misra R ,Wijesuriya M, Banerjee D. The metabolic syndrome in South Asians : continuing escalation and possible solutions.Indian J Med Res 2007;125:345-54.

258. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415-28.

259. Murakami T, Michelagnoli S,Loughi R,et al.Triglycerides are major determinants of cholesterol esterification/ transfer and HDL remodelling in human plasma. Arterioscler Thromb Vas Boil 1995;15:1819-28.

260 .Misra A,Wasir JS,Pandey RM.An elevation of candidate definition of the metabolic syndrome in adult Asian Indians. Diabetes Care 2005; 28:398-403.

260. Rajat J. Gaiha M, Chakravarthi AL, Daga MK. Insulin resistance/hyperinsulinemia as a risk factor for common carotid artery intima/media thickness in essential hypertension. JIACM 2005;6(2):122-8.

261. Munja YP. Metabolic syndrome-a useful concept.chapter -32 in: RK Singal. Medicine update:Jaypee Publishers 2007 ;17:185-9.

Age	Gender	SVD	DVD	TVD	Smoking	Alcohol	Family History	BP	FBS	TGL	HDL	WC	DM	CAD	SHT	DYSLIPIDEMIA	OBESITY	HYPOTHYROID	ANAEMIA	HYPERHOMOCYSTINEMIA	PVOD	MS	ST Elevation	LVD
43	1	0	1	0	1	1	0	1	1	149	37	97	1	1	1	1	0	0	0	0	0	1	1	1
45	1	1	0	0	1	1	0	0	1	138	32	91	1	1	0	0	0	0	0	0	0	1	1	0
40	1	1	0	0	1	1	0	1	1	178	33	113	1	1	1	0	0	0	0	0	0	1	0	1
37	1	1	0	0	0	0	0	1	1	527	38	93	1	0	1	0	0	0	0	0	0	1	0	0
37	1	1	0	0	0	0	0	1	0	206	50	97	0	0	0	0	0	0	0	0	0	1	1	0
45	1	0	0	1	0	0	0	1	1	98	32	99	1	0	1	0	0	0	0	0	0	1	1	1
43	1	1	0	0	1	1	0	1	1	112	30	97	0	0	1	0	0	0	0	0	0	1	1	0
45	1	1	0	0	1	1	0	0	1	114	38	99	1	0	0	0	0	0	0	0	0	1	1	0
38	1	1	0	0	0	1	1	1	0	106	19	90	0	0	0	0	0	0	0	0	0	1	1	0
30	1	0	1	0	1	1	1	1	1	179	32	94	1	0	0	0	0	0	0	0	0	1	1	0
41	1	0	1	0	1	1	1	1	1	214	26	92	1	0	0	0	0	0	0	0	0	1	1	0
42	1	1	0	0	1	1	0	0	1	170	42	90	1	0	0	0	0	0	0	0	0	1	0	0
43	1	0	1	0	0	1	0	0	0	132	41	83	0	0	0	1	0	0	0	0	0	0	1	0
31	1	1	0	0	1	1	0	0	0	212	41	96	0	0	0	0	0	0	0	0	0	1	0	0
37	1	0	1	0	1	1	0	0	1	164	30	102	1	0	0	0	0	0	0	0	0	1	0	0
36	1	1	0	0	1	1	0	0	0	119	37	86	0	0	0	0	0	0	0	0	0	0	0	1
42	1	1	0	0	1	1	0	1	1	58	50	100	1	0	1	0	0	0	0	0	0	1	1	0
37	1	1	0	0	1	1	0	0	1	233	35	93	1	0	0	0	0	0	0	0	0	1	1	0
42	1	0	1	0	0	1	0	1	0	64	37	112	0	0	0	0	0	0	0	0	0	1	1	1
45	1	1	0	0	1	0	1	1	1	69	26	110	0	0	1	0	0	1	0	0	0	1	1	0
33	1	1	0	0	0	0	0	0	1	310	48	86	1	0	0	0	0	0	0	0	0	1	1	1
38	1	0	1	0	1	0	0	1	0	282	28	104	0	0	1	0	0	0	0	0	0	1	1	0
41	1	1	0	0	0	0	0	0	1	93	55	79	1	0	0	0	0	0	0	0	0	0	1	0
34	1	0	0	1	1	0	0	1	1	411	24	93	1	0	0	0	0	0	0	0	0	1	0	0
29	1	1	0	0	0	0	0	1	0	136	28	108	0	0	0	0	0	0	0	0	0	1	1	0
40	1	0	1	0	1	0	0	0	1	124	22	78	1	0	0	0	0	0	0	0	0	0	1	1
43	1	0	0	1	1	0	0	1	1	157	16	99	1	0	1	0	0	0	0	0	0	1	0	1
41	0	0	0	1	0	0	0	0	1	80	46	89	1	0	0	0	0	0	0	0	0	1	0	0
45	1	0	0	1	1	0	0	1	1	153	25	109	1	0	1	1	0	0	0	0	0	1	1	1

Age	Gender	SVD	DVD	TVD	Smoking	Alcohol	Family History	BP	FBS	TGL	HDL	WC	DM	CAD	SHT	DYSLIPIDEMIA	OBESITY	HYPOTHYROID	ANAEMIA	HYPERHOMOCYSTINEMIA	PVOD	MS	ST Elevation	LVD
40	1	0	0	1	0	0	0	1	0	89	38	90	0	0	1	0	0	0	0	0	0	1	0	1
40	1	0	0	1	0	1	0	1	0	109	30	94	0	0	1	0	0	0	0	0	0	1	0	0
38	1	1	0	0	1	1	0	1	0	105	26	94	0	0	1	0	0	0	0	0	0	1	0	1
45	1	1	0	0	0	0	1	1	1	179	48	106	1	0	1	0	0	0	0	0	0	1	0	0
44	1	1	0	0	1	1	1	1	0	364	22	93	0	0	1	0	0	0	0	0	0	1	1	0
34	1	0	1	0	1	1	0	1	0	151	41	108	0	0	1	1	0	0	0	0	0	1	0	0
40	1	0	1	0	1	0	0	0	0	41	41	88	0	0	0	0	0	0	0	0	0	0	1	0
41	1	1	0	0	1	1	0	0	0	125	32	88	0	0	0	0	0	0	0	0	0	0	1	0
45	1	0	0	1	1	0	0	1	1	140	40	103	1	0	1	1	0	0	0	0	0	1	1	1
41	1	1	0	0	1	1	0	0	0	69	33	75	0	0	0	0	0	0	0	0	0	0	1	0
41	1	1	0	0	1	1	0	1	1	88	29	109	1	0	1	0	0	0	0	0	0	1	0	0
41	1	1	0	0	0	0	1	0	1	181	52	94	1	0	0	1	0	0	0	0	0	1	0	0
44	1	1	0	0	1	0	0	1	1	120	31	107	1	0	1	0	0	0	0	0	0	1	1	1
39	0	1	0	0	0	0	0	1	0	285	33	83	0	0	0	0	0	0	0	0	0	1	0	0
40	1	0	1	0	1	1	0	1	0	84	40	88	0	0	1	0	0	0	0	0	0	0	0	1
42	1	0	1	0	0	0	0	0	1	163	28	96	1	0	1	0	0	0	0	0	0	1	0	0
40	0	1	0	0	0	0	0	1	1	116	29	72	1	0	1	0	0	0	0	0	0	0	1	0
37	1	1	0	0	1	1	0	1	0	354	43	99	0	0	1	1	0	0	0	0	0	1	1	1
38	1	1	0	0	1	1	0	1	1	106	37	94	0	0	1	0	0	0	0	0	0	1	0	0
45	1	1	0	0	1	0	1	0	0	101	28	107	0	0	0	1	0	0	0	0	0	1	1	0
43	1	1	0	0	1	1	0	1	0	133	22	90	0	0	1	1	0	0	0	0	0	1	0	0
42	1	0	1	0	0	0	0	0	1	86	37	98	1	0	0	1	0	0	0	0	0	1	0	0
38	1	1	0	0	1	0	1	0	0	415	18	108	0	0	0	0	0	0	0	0	0	1	0	0
32	1	0	1	0	1	1	0	0	0	113	35	84	0	0	0	0	0	0	0	0	0	0	0	0
43	1	1	0	0	1	1	0	0	1	144	32	99	1	0	0	0	0	0	0	0	0	1	0	0
30	1	1	0	0	1	1	0	0	0	190	48	87	0	0	0	0	1	0	0	0	0	0	1	1
42	1	1	0	0	0	0	1	0	1	141	42	88	1	0	0	0	0	0	0	0	0	0	1	0
37	1	1	0	0	1	1	0	0	1	136	33	85	0	0	0	0	0	0	0	0	0	0	1	1
45	1	0	0	1	1	1	0	1	1	242	25	106	1	0	1	0	0	0	0	0	0	1	1	1

Age	Gender	SVD	DVD	TVD	Smoking	Alcohol	Family History	BP	FBS	TGL	HDL	WC	DM	CAD	SHT	DYSLIPIDEMIA	OBESITY	HYPOTHYROID	ANAEMIA	HYPERHOMOCYSTINEMIA	PVOD	MS	ST Elevation	LVD
42	1	0	1	0	0	0	0	1	1	90	53	88	1	0	0	0	0	0	0	0	0	0	1	1
44	0	0	0	1	0	0	0	1	1	140	22	90	1	0	1	0	0	1	1	0	0	1	0	1
28	1	1	0	0	1	1	0	1	0	96	30	112	0	0	1	0	0	0	0	0	0	1	1	1
41	0	1	0	0	0	0	0	0	1	145	37	85	1	0	0	1	0	0	0	0	0	1	0	0
30	1	1	0	0	1	1	0	0	1	134	15	82	0	0	0	0	0	0	0	1	0	0	1	1
45	1	1	0	0	0	0	0	1	0	229	20	94	0	0	0	0	0	0	0	0	0	1	1	0
42	1	0	0	1	0	0	0	1	1	291	24	90	0	0	0	0	0	0	0	0	0	1	0	1
45	0	0	1	0	0	0	0	1	1	152	37	88	1	0	0	0	0	0	0	0	0	1	0	0
44	1	1	0	0	1	1	0	0	1	226	29	94	0	0	0	1	0	0	0	0	0	1	1	1
26	1	1	0	0	0	0	0	0	0	85	40	86	0	0	0	0	0	0	0	0	0	0	0	0
39	1	1	0	0	0	0	0	1	1	169	17	93	1	0	0	1	0	0	0	0	1	1	1	1
38	1	1	0	0	1	1	0	0	0	167	37	96	0	0	0	0	0	0	0	0	0	1	1	0
36	1	1	0	0	1	1	0	1	1	97	24	90	1	0	1	0	0	0	0	0	0	1	1	0
41	1	0	1	0	1	1	0	1	0	167	32	114	0	0	1	0	1	0	0	0	0	1	0	0
41	1	1	0	0	1	0	0	0	0	182	25	96	0	0	0	1	0	0	0	0	0	1	1	0
41	1	1	0	0	0	1	0	1	1	183	29	95	1	0	0	0	0	0	0	0	0	1	1	0
37	1	1	0	0	1	0	0	1	0	121	34	93	0	0	0	0	0	0	0	0	0	1	1	1
44	1	1	0	0	1	1	1	0	1	129	32	100	0	0	0	0	0	0	0	0	0	1	1	1
36	1	1	0	0	1	1	0	0	1	49	60	79	0	0	0	0	0	0	0	1	0	0	1	1
45	1	0	1	0	0	0	0	0	1	101	34	91	1	0	0	1	0	0	0	0	0	1	0	1
42	1	0	1	0	1	1	0	0	1	389	20	76	1	0	0	1	0	0	0	0	0	0	0	0
41	1	0	1	0	1	0	0	1	1	73	29	91	1	0	0	0	0	0	0	0	0	1	0	1
43	1	0	0	1	1	1	0	1	1	80	42	95	1	1	1	0	0	0	0	0	0	1	1	1
30	1	1	0	0	1	0	0	0	0	89	29	85	0	0	0	0	0	0	0	1	0	0	1	1
26	1	1	0	0	0	0	0	1	0	175	31	85	0	0	0	0	0	0	0	0	0	0	1	1
40	1	1	0	0	0	0	0	1	1	143	26	89	0	0	1	1	0	0	0	0	0	0	1	0
42	1	1	0	0	0	0	0	0	0	170	31	90	0	0	0	0	0	0	0	0	0	1	1	0
37	1	1	0	0	1	1	1	0	1	372	42	91	1	0	0	0	0	0	0	0	0	1	1	0
43	1	0	0	1	1	1	0	1	0	100	42	82	0	0	1	0	0	0	0	0	0	0	1	1

Age	Gender	SVD	DVD	TVD	Smoking	Alcohol	Family History	BP	FBS	TGL	HDL	WC	DM	CAD	SHT	DYSLIPIDEMIA	OBESITY	HYPOTHYROID	ANAEMIA	HYPERHOMOCYSTINEMIA	PVOD	MS	ST Elevation	LVD
44	1	1	0	0	1	0	0	0	0	157	29	79	0	0	0	0	0	0	0	0	0	0	1	0
45	0	0	0	1	0	0	0	1	0	241	44	96	0	0	1	0	0	0	0	0	0	1	0	0
45	1	0	0	1	1	0	0	0	1	168	27	91	0	0	0	0	0	0	0	0	0	1	0	0

Gender: 1=male,0=female

Smoking: 1=smoker,0=non-smoker

Alcohol: 1=alcoholic,0=non-alcoholic

SVD:1=Present,0=Absent

DVD: 1=Present,0=Absent

TVD:1=Present,0=Absent

FBS: 1=Fasting blood sugar ≥100mg/dl:0=Fasting blood sugar <1(

SHT:1=Blood pressure>130/85mmHg:0=Blood pressure <135/85

DM: 1=Kown diabetic:0=Non-Diabetic

Dyslipidemia:1=present already,0-Absent

Anemia 1=present ,0-Absent

Hyperhomocystinemia: 1=present,0-Absent

Hypothyroid: 1=present,0-Absent

PVOD:1=present ,0-Absent

Obesity:1=present ,0-Absent

MS(metabolic syndrome:1=present,0-Absent

LVD(Left Ventricular Dysfunction -EF<50%)1=present ,0-Absent

STEMI(ST-elevation MI):1=present ,0-Absent

PROFORMA

Case NO. :

Name :

Age :

Sex :

IP. NO :

Occupation :

1. Chief Complaints:

2. Past History: Diabetes mellitus

Hypertension

IHD

3. Family History: Coronary Artery Disease

Diabetes mellitus

Hypertension

4. Personal History: Current smoking – Y/N

Alcohol consumption – Y/N

5. Blood Pressure

6. Waist Circumference

7. FBS

8. Triglycerides

9. HDL – C

10. Cardiac Enzymes

11. ECG

12. Echo

13. Coronary Angiogram

CONSENT FORM

சு வருண் ஆகிய நான், PSG மருத்துவக் கல்லூரியின் பொது மருத்துவ துறையின் கீழ் "இளம் வயதில் மாரடைப்பால் பாதிக்கப்பட்டவர்களில் மெட்டபாலிக் சின்ரோம்மின் தாக்கம் பற்றிய தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி: மரு. சுஜயா மேனன்

ஆய்வு மேற்கொள்வதற்கான அடிப்படை: இந்த ஆய்வின் மூலம் "இளம் வயதில் மாரடைப்பால் பாதிக்கப்பட்டவர்களில் மெட்டபாலிக் சின்ரோம்மின் தாக்கம் உள்ளதா என கண்டறிய முடியும். இதன் மூலம் திட்டங்கள் வருத்து எதிர்காலத்தில் இளம் வயதில் மாரடைப்பு வருவதை முன்கூட்டியே தவிர்க்க இயலும்.

ஆய்வு மேற்க்கொள்ளும் இடம்- PSG IMS & R

ஆய்வின் விவரம்: இந்த ஆய்வில் மெட்டபாலிக் சின்ரோம்மின் காரணிகளைப் பற்றி சில வினாக்கள் உங்களிடம் கேட்கப்படும். பின்னர் 5 ml இரத்தம் உங்களிடமிருந்து எடுத்து உங்களின் சர்க்கரை மற்றும் கொழுப்பின் அளவு கண்டறியப்படும். பின்னர் உங்கள் இடுப்பின் சுற்றளவு அளக்கப்படும். இதற்கு உங்கள் சம்மதமும் ஒத்துழைப்பும் கோருகிறேன்.

ஆய்வினால் ஏற்படும் அசௌகரியங்கள் / பக்க விளைவுகள்: இரத்த மாதிரி 5ml எடுக்கும் நேரத்தில் சிறிது வலி ஏற்படும். ஆனால் அது சிறிது நேரத்தில் சரியாகி விடும். இந்த ஆய்வில் பங்கேற்பதும், மேற்கொண்டு தொடருவதும் உங்கள் விருப்பம், இதனால் உங்கள் மருத்துவ சிகிச்சையில் எந்த பாதிப்பும் ஏற்படாது.

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் 5 வருடங்கள் பாதுகாக்கப்படும். இவை வேறு எந்த ஆய்விற்கும் பயன்படுத்தப் படமாட்டாது. எந்த நிலையிலும் உங்களைப் பற்றிய தகவல்கள் யாருக்கும் தெரிவிக்கப்பட மாட்டாது. அவை இரகசியமாக வைக்கப்படும்.

IHEC contact No: 0422 2570170 Extn: 5818

CONSENT FORM

I, **PSG Institute of Medical Science and Research, Coimbatore Institutional Human Ethics Committee**

INFORMED CONSENT FORMAT FOR STUDENT RESEARCH PROJECTS

I / We (write name of the Student investigator(s) here) S.varun **Post graduate M.D (General Medicine), 2012 batch** (course and year of admission, batch [Regular or Additional]) students of the PSG Institute of Medical Sciences & Research (PSG IMS&R), **am /** are carrying out a study on the topic:

A STUDY ON PREVALENCE OF METABOLIC SYNDROME IN PREMATURE CORONARY ARTERY DISEASE PROVEN BY CORONARY ANGIOGRAM as part of my / our student research project being carried out under the aegis of the Department of General Medicine.

My /Our research guide is Dr.SUJAYA MENON ; **Designation:** Professor, Department of General Medicine, My co- guide is Dr. G. Rajendiran Professor, HOD, Department of Cardiology PSG IMSR.

The justification for this study is Though studies have revealed that the presence of metabolic syndrome constitutes around 6 fold increase in the cardio vascular mortality, the levels of increased risk have not been clearly defined that too in younger age group. The increased risk of morbidity and mortality associated with metabolic syndrome makes it essential in understanding the dimension of this syndrome for allocation of health care and research resources and for other purposes .These traditional risk factors all together accounts for approximately half of the risk of first myocardial infarction, especially in the Asian Indian population. However both incident and prevalence of CVD will likely to increase in the next decades with significant socio-economic consequences ,very few studies have reported on the prevalence of metabolic syndrome in the native Indian population based on epidemiological studies and almost no studies been conducted on its prevalence in younger age group .This is particularly relevant as india has the maximum number of diabetes patients , hence early intervention of this metabolic syndrome with intensive lifestyle modifications in the form of diet, exercises and drugs would definitely

prevent future development of CVD like myocardial infarction and this study will definitely helpful in establishing primary prevention strategies.

The aim of this study is:

To evaluate the prevalence of metabolic syndrome in premature coronary artery disease proven by coronary angiogram using IDF criteria.

Sample size: 90 patients.

Respondents are (population group & .age group): patients who have been diagnosed as premature coronary artery disease .

Location: PSG IMSR.

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out (strike off items that are not applicable):

Initial interview (specify approximate duration): 20 minutes.

Health education sessions: Number of sessions- ONE.

Approximate duration of each session: 10 minutes.

Clinical examination (Specify details and purpose): YES. General and system wise examination as a part of routine work up.

Blood sample collection: Specify quantity of blood being drawn:~5ml

Purpose- To estimate fasting TGL,HDL & Blood sugar.Discomfort- Minimal pain while drawing blood sample.

Medication given, if any, duration, side effects, purpose, benefits: NIL

Final interview (specify approximate duration):NIL

If photograph is taken, purpose: NO

Benefits from this study, if any: .Helps us to know the present status of distribution of metabolic syndrome among premature coronary artery disease population and make us plan early primary prevention strategies towards at risk population in preventing complications.

How the results will be used: Study will be submitted to "The Tamil Nadu DR. M.G.R Medical University" as a part of PG thesis.

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the student investigators from the PSG IMS&R. Having understood the same, I hereby give my consent to them to interview me. I affixing my signature / left thumb impression to indicate my consent and willingness to cooperate in this study.

Respondent ID: _____.

Signature / Left thumb impression of the Respondent.

Signature of the Interviewer with date

IHEC CONTACT NUMBER: 0422 2570170, Extn-5818

ABBREVIATIONS

ACS	-	Acute Coronary Syndrome
ADA	-	American Diabetes Association
ACC	-	American College of Cardiology
BMI	-	Body Mass Index
CAD	-	Coronary Artery Disease
CRP	-	C Reactive Protein
CVD	-	Cardio Vascular Disease
CURES	-	Chennai Urban Rural Epidemiology Study
DECODE	-	Diabetes Epidemiology:Collaborative analysis Of Diagnostic criteria in Europe
ESC	-	European Society of Cardiology
FRS	-	Framingham Risk Score
ID	-	Implantable Defibrillator
IRS	-	Insulin Response Syndrome
IDF	-	International Diabetes Federation
LVD	-	Left Ventricular Dysfunction
METS/MS	-	Metabolic Syndrome
MI	-	Myocardial Infarction
NSTEMI	-	Non ST Segment Elevation MI
NHLBI	-	National Heart Lung And Blood Institute

PAR	-	Population Attributable Risk
PAI 1	-	Platelet Adhesion Inhibition 1
PCI	-	Precutaneous Coronary Intervention
RCA	-	Right Coronary Artery
SERCA 2a	-	Sarcoplasmic Reticulum Ca^{2+} Atpase
SHT	-	Systemic Hyper Tension
SNP	-	Single Nucleotide Polymorphisim
SAVE	-	Survival And Ventricular Enlargement
UKDAS	-	United Kingdom Asian Diabetic Study
WHO	-	World Health Organisation
WC	-	Waist Circumference
WHR	-	Waist Hip Ratio